

The Daily COVID-19 Literature Surveillance Summary

July 6, 2020



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COVID-19 Daily Literature Surveillance

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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	Non-randomized controlled cohort/follow-up study**	Case-series, case-control or historically controlled studies**	Mechanism-based reasoning
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>

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EXECUTIVE SUMMARY

Climate:

- A cross-sectional study (n=72,417 from 27 countries) found that [elderly people \(ages 60-80\) reported less compliance with preventative measures](#) against COVID-19 such as mask wearing, despite this population being at highest risk for severe disease and government interventions specifically targeting them. This suggests governments may need to revise their current strategies to promote preventative measures in elderly populations.
- A qualitative focus group in Australia found that community members agree there is a [“degree” of responsibility for paramedics to continue working through the COVID-19 pandemic](#) but were ambivalent on if that obligation applies to crisis care beyond routine operations. Several recurring themes include context of obligation, acceptable risk, access to PPE, and legal and ethical guidelines. The authors propose a “Crisis Standards of Care” consensus to define the legal and ethical bounds for healthcare professionals during times of crisis.
- [Serial testing of 98 incarcerated or detained individuals with known COVID-19 exposure](#) in a Louisiana correctional facility identified a large number of asymptomatic and presymptomatic cases that were not originally identified through symptom screening. The authors conclude that rapid detection, serial testing, cohorting, and isolation of COVID-19-infected individuals and their close contacts are all important to reduce SARS-CoV-2 transmission in congregated settings and, by extension, the outside community.

Epidemiology:

- Modeling and mechanism-based research include the following:
 - [If transmission is highly dependent on those with active symptoms](#), countries with older populations are likely to have the highest reproductive numbers, while if transmission is equal between symptomatic and asymptomatic cases, countries with younger populations will have the highest reproductive ratios.
 - Of the estimated [87,000 excess deaths in the US from COVID-19](#), only 56,246 were a direct result of disease, while increased death from heart disease (89%), cerebrovascular disease (35%), Alzheimer's (64%), and diabetes (96%) likely represent indirect mechanisms of increased mortality during the pandemic.
 - The [transition from sub-exponential to exponential transmission](#) occurs eight weeks after the first case cluster, and likely depends on early public health responses, such as limiting spread on public transit in major metropolitan areas.
- A CDC multi-state telephone survey of 350 adult inpatients and outpatients who had a positive SARS-CoV-2 test found [inpatients were more likely to be older, minorities, and from lower socioeconomic groups](#). Also, 46% of participants reported close contact with an infected individual (most commonly a family member [45%] or work colleague [34%]) suggesting that increased screening and contact tracing are necessary to control the R₀.
- This ecological study in 38 European nations found a [negative association between prevalence of smoking and COVID-19 cases](#) ($p<0.0001$) and no direct association between smoking prevalence and COVID-19 mortality ($p=0.6260$)
- This retrospective cohort study from 2 academic hospitals in New York City found that [COVID-19 patients were more likely to have an acute ischemic stroke than influenza A/B patients](#) ($n = 1486$) ($OR\ 7.6$; 95% CI, 2.3-25.2), further implicating a unique hypercoagulable state in COVID-19 disease.

Understanding the Pathology:

- A study of 6 severely ill and 6 recovering COVID-19 patients in China period found that [higher disease severity](#) was associated with increased CD4+ and CD8+ T cells, higher levels of sydecans-1 and interleukin-6 (IL-6), and increased neutralizing antibodies correlated with disease remission.
- [In-vitro experiments at Johns Hopkins University](#) detected expression of the ACE-2 receptors in neuronal cells, SARS-CoV-2 presence in neurons, and increased viral replication in neural cell lysate 72 hours post infection suggesting a possible mechanism for direct CNS injury in COVID-19.

Transmission and Prevention:

- A [review of COVID-19 vaccine development](#) reports the majority of potential vaccines are intended to induce a neutralizing antibody response against the SARS-CoV-2 spike [S] protein, and the American “Warp Speed” program now has five front-line vaccine candidates based on mRNA or adenovirus vectors. Authors suggest that aggressive timelines due to urgency of need, adequate vaccine trials, and manufacturing and distribution are among the greatest challenges faced in vaccine development.
- A [retrospective cohort study of 11,580 contacts](#) of COVID-19 cases in Guangdong, China found that 4.4% of contacts were infected with SARS-CoV-2, and risk of infection was highest in children and the 60-69 age range. They also found higher transmission with prolonged exposure during the symptomatic period of disease.

Management:

- A review of 12 reports of 90 patients in China who [re-tested positive for SARS-CoV-2 via RT-PCR testing after discharge](#) found that these patients were largely asymptomatic and re-tested positive despite proper discharge protocol (i.e. 2 negative results for SARS-CoV-2 RT-PCR 24 hours apart). Although the reasons for this phenomenon remain uncertain, the authors suggest testing respiratory and fecal samples simultaneously when discharging COVID-19 patients and educating patients on post-discharge quarantine, social distancing, and appropriate follow-up protocol.
- A [retrospective cohort study](#) conducted from 2 New York hospitals found that of the 38 COVID-19 patients who underwent tracheostomies 55% of patients (n=21) had weaned from ventilators, 18.4% had undergone decannulation (n=7), and 5.3% expired for reasons unrelated to surgery (n=2); no surgeons seroconverted. This suggests tracheostomy may be a safe and effective way to improve outcomes in respiratory failure.

R&D Diagnosis and Treatment:

- A prospectively study of 106 COVID-19 patients in Italy found that [the volume of disease on CT was a predictor of short-term outcomes, while CRP better predicted the volume of disease](#) ($p<0.001$). Therefore, these clinical markers may be useful for patient risk assessment when RT-PCR results cannot be quickly obtained.
- [Automated chemiluminescent immunoassays \(CLIA\) for SARS-CoV-2](#) were developed and evaluated at 10 Chinese hospitals (972 patients and 586 community donor samples). They found the clinical sensitivity of IgM was 82.54, 92.93, and 84.62% before 7 days, 7-14 days, and after 14 days respectively, since onset of symptoms, and SARS-CoV-2 IgG showed clinical sensitivity of 80.95, 97.98, and 99.15%. This adds another potential diagnostic test for COVID-19 infection that the authors believe can be more accurate than current nucleic acid testing.

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ELDERLY PEOPLE AND RESPONSES TO COVID-19 IN 27 COUNTRIES

Daoust JF.. PLoS One. 2020 Jul 2;15(7):e0235590. doi: 10.1371/journal.pone.0235590. eCollection 2020.

Level of Evidence: 3 - Local non-random sample

BLUF

A cross-sectional study (n=72,417 from 27 countries) by an author affiliated with the University of Edinburgh found that self-reported compliance scores with preventative measures against COVID-19 does not correlate with age (Figure 3), despite government interventions specifically targeting elderly individuals. When comparing specific preventive measures, age and compliance for mask-wearing were found to have a negative correlation, with an observable drop in compliance score between the ages of 60 to 80 (Figure 4). These findings suggest that governments may need to revise their current strategies to better promote preventative measures in elderly populations.

ABSTRACT

Amongst the most robust consensus related to the COVID-19 disease is that the elderly are by far the most vulnerable population group. Hence, public authorities target older people in order to convince them to comply with preventive measures. However, we still know little about older people's attitudes and compliance toward these measures. In this research, I aim to improve our understanding of elderly people's responses to the pandemic using data from 27 countries. Results are surprising and quite troubling. Elderly people's response is substantially similar to their fellow citizens in their 50's and 60's. This research (i) provides the first thorough description of the most vulnerable population's attitudes and compliance in a comparative perspective (ii) suggest that governments' strategies toward elderly people are far from successful and (iii) shows that methodologically, we should be more cautious in treating age as having a linear effect on COVID-19 related outcomes.

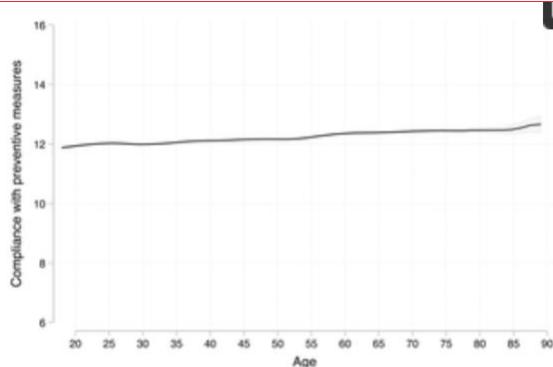
FIGURES

Fig 3. Compliance with preventive measures and age. Local regression with a kernel (epanechnikov) function and a bandwidth of 0.8, with 84% confidence intervals included. [19].

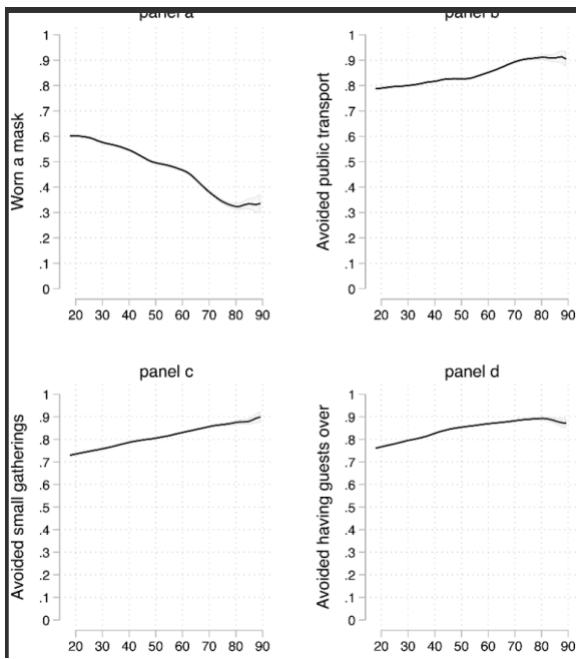


Fig 4. The effect of age on particular preventive measures. Local regression with a kernel (epanechnikov) function and a bandwidth of 0.8, with 84% confidence intervals included. [19].

TO PUNISH OR TO ASSIST? DIVERGENT REACTIONS TO INGROUP AND OUTGROUP MEMBERS DISOBEDIING SOCIAL DISTANCING

Van Assche J, Politi E, Van Dessel P, Phalet K.. Br J Soc Psychol. 2020 Jun 30:e12395. doi: 10.1111/bjso.12395. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

BLUF

Researchers at the University of Leuven, Belgium had Britons (N=377) read a scenario (norm-conforming or norm-violating) about the behavior of a target group (in- or out-group) and complete an assessment of "moral emotions" and support for solidarity-based (assistance) or punishment-based (retributive) measures. Researchers found that participants were in favor of assistance over retributive measures ($p<.001$, Figure 1), while those in the norm-violating condition reported less positive/more negative moral emotions toward both in-group (Britons) and out-group (Italians) members (Figure 2). Negative emotions were overall associated with support for punishment-based measures. Authors suggest that norm deviation may serve as justification for out-group disparagement, and differences in support of in- and out-groups could lead to out-group blaming and worsen international tensions. They urge for inclusivity of social identities to promote collective resilience and international solidarity, which was shown to be endorsed by participants.

ABSTRACT

In response to the COVID-19 pandemic, societies face the formidable challenge of developing sustainable forms of sociability-cumsocial-distancing - enduring social life while containing the virus and preventing new outbreaks. Accordant public policies often balance between retributive (punishment-based) and assistance (solidarity-based) measures to foster responsible behaviour. Yet, the uncontrolled spreading of the disease has divided public opinion about which measures are best suited, and it has made salient group disparities in behaviour, potentially straining intergroup relations, elevating heated emotions, and undercutting coordinated international responses. In a 2×2 between-subjects experiment, British citizens (N = 377) read about national in-group or outgroup members (categorical differentiation), who were either conforming to or deviating from the corona regulations (normative differentiation). Participants then reported moral emotions towards the target national group and indicated support for public policies. In general, support for assistance policies outweighed support for retributive measures. Second, however, norm deviation was associated with less positive and more negative moral emotions, the latter category further relating to more punitiveness and less assistance support. Finally, respondents who read about norm-violating outgroup members especially reported support for retributive measures, indicating that people might use norm deviation to justify outgroup derogation. We discuss implications for policymakers and formulate future research avenues.

FIGURES

TODO: ERROR EMBEDDING IMAGE: https://covid19lst.qualtrics.com/jfe/file/F_2E4qgBd1Z70Eg9G

Figure 1: Mean plots (with 95% confidence interval error bars) of the effects of normative and categorical differentiation on support for retributive (a) and assistance measures (b) to contain the virus.

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Figure 2: Unstandardized results (standard errors between brackets) of the models testing the effect of normative and categorical differentiation on support for retributive (a) and assistance measures (b) to contain the virus via moral emotions.

Note. *p<.05; **p<.01; ***p<.001.

AFFECTING THE HEALTHCARE WORKFORCE

DO PARAMEDICS HAVE A PROFESSIONAL OBLIGATION TO WORK DURING A PANDEMIC? A QUALITATIVE EXPLORATION OF COMMUNITY MEMBER EXPECTATIONS

Anderson C, Pooley JA, Mills B, Anderson E, Smith E.. Disaster Med Public Health Prep. 2020 Jun 24:1-24. doi: 10.1017/dmp.2020.212. Online ahead of print.

Level of Evidence: Other - Expert Opinion

BLUF

A qualitative focus group study found that 41 participants who were community members age 18 years or older in Victoria, Australia felt there was a “degree” of responsibility for paramedics to continue working through the COVID-19 pandemic, but were ambivalent on whether paramedics have an obligation to respond to crisis care beyond routine operations. Discussions within the four focus groups shared several recurring themes, including context of obligation, risk acceptability, access to PPE, and legal and ethical guidelines (Tables 1 and 2). The authors suggest that a “Crisis Standards of Care” should be in place to define the legal and ethical bounds for healthcare professionals during times of crisis.

ABSTRACT

OBJECTIVE: Previous research has identified a lack of clarification regarding paramedic professional obligation to work. Understanding community expectations of paramedics will provide some clarity around this issue. The objective of this research was to explore the expectations of a sample of Australian community members regarding the professional obligation of paramedics to respond during pandemics. **METHODS:** The authors employed qualitative methods to gather Australian community member perspectives immediately prior to the onset of the COVID-19 pandemic. Focus groups were used for data collection, and a thematic analysis conducted. **RESULTS:** The findings revealed nine key themes: context of obligation (normal operations versus crisis situation); hierarchy of obligation (individual versus organizational obligation); risk acceptability; acceptable occupational risk (it's part of the job); access to PPE; legal and ethical guidelines; education and training; safety; and acceptable limitations to obligation. The factors identified as being acceptable limitations to professional obligation are presented as further sub-themes: physical health; mental health; and competing personal obligations. **CONCLUSION:** The issue of professional obligation must be addressed by ambulance services as a matter of urgency, especially in light of the COVID-19 coronavirus pandemic. Further research is recommended to understand how community member expectations evolve during and after the COVID-19 coronavirus pandemic.

FIGURES

Themes	Sub-themes
Context of obligation	Does the same professional obligation transcend normal operations into crisis situations?
Hierarchy of obligation	Obligations of individual paramedics versus organizational obligation to protect workers.
Risk acceptability	Determining level of risk acceptability; ramifications; managing risk that breaches a risk-acceptability threshold; controlled versus uncontrolled risk; timing of paramedic risk acceptability decisions.
Acceptable occupational risk	Expectation that a certain degree of risk is inherently 'part of the job'.
Access to PPE	Paramedic professional obligation dependent on access to appropriate PPE.
Legal and ethical guidelines	Ethical versus legal obligation.
Education and training	Expectation that with specialized education comes obligation to respond.
Safety	Acceptability of physical risk versus health risk.
Acceptable limits to obligation	Physical health; mental health; competing personal obligations.

Table 1. Identified themes and sub-themes

Physical health issues	Mental health issues	Competing obligations
Pregnant females; Pre-existing chronic illness; Paramedics who become infected during the pandemic	Pre-existing mental health issues; Mental health issues that develop during course of pandemic (e.g. PTSD)	Single parents; Parents of children with chronic illness; Both parents are healthcare workers

Table 2. Examples of acceptable limitations on professional responsibility

DISPARITIES

SERIAL LABORATORY TESTING FOR SARS-COV-2 INFECTION AMONG INCARCERATED AND DETAINED PERSONS IN A CORRECTIONAL AND DETENTION FACILITY - LOUISIANA, APRIL-MAY 2020

Njuguna H, Wallace M, Simonson S, Tobolowsky FA, James AE, Bordelon K, Fukunaga R, Gold JAW, Wortham J, Sokol T, Haydel D, Tran H, Kim K, Fisher KA, Marlow M, Tate JE, Doshi RH, Curran KG.. MMWR Morb Mortal Wkly Rep. 2020 Jul 3;69(26):836-840. doi: 10.15585/mmwr.mm6926e2.

Level of Evidence: 3 - Local non-random sample

BLUF

A morbidity and mortality weekly report from the CDC and Louisiana Department of Health describes serial testing of 98 incarcerated or detained individuals quarantined with known COVID-19 exposure in a Louisiana correctional and detention

facility. They identified a large number of asymptomatic and presymptomatic cases that were not originally identified through symptom screening. The authors conclude that rapid detection, serial testing, cohorting, and isolation of COVID-19-infected individuals and their close contacts are all important to reduce SARS-CoV-2 transmission in congregate settings and, by extension, the outside community.

ABSTRACT

Transmission of SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19), by asymptomatic and presymptomatic persons poses important challenges to controlling spread of the disease, particularly in congregate settings such as correctional and detention facilities (1). On March 29, 2020, a staff member in a correctional and detention facility in Louisiana developed symptoms and later had a positive test result for SARS-CoV-2. During April 2-May 7, two additional cases were detected among staff members, and 36 cases were detected among incarcerated and detained persons at the facility; these persons were removed from dormitories and isolated, and the five dormitories that they had resided in before diagnosis were quarantined. On May 7, CDC and the Louisiana Department of Health initiated an investigation to assess the prevalence of SARS-CoV-2 infection among incarcerated and detained persons residing in quarantined dormitories. Goals of this investigation included evaluating COVID-19 symptoms in this setting and assessing the effectiveness of serial testing to identify additional persons with SARS-CoV-2 infection as part of efforts to mitigate transmission. During May 7-21, testing of 98 incarcerated and detained persons residing in the five quarantined dormitories (A-E) identified an additional 71 cases of SARS-CoV-2 infection; 32 (45%) were among persons who reported no symptoms at the time of testing, including three who were presymptomatic. Eighteen cases (25%) were identified in persons who had received negative test results during previous testing rounds. Serial testing of contacts from shared living quarters identified persons with SARS-CoV-2 infection who would not have been detected by symptom screening alone or by testing at a single time point. Prompt identification and isolation of infected persons is important to reduce further transmission in congregate settings such as correctional and detention facilities and the communities to which persons return when released.

ESTIMATION OF COUNTRY-LEVEL BASIC REPRODUCTIVE RATIOS FOR NOVEL CORONAVIRUS (SARS-COV-2/COVID-19) USING SYNTHETIC CONTACT MATRICES

Hilton J, Keeling MJ.. PLoS Comput Biol. 2020 Jul 2;16(7):e1008031. doi: 10.1371/journal.pcbi.1008031. Online ahead of print.
Level of Evidence: Other - Modeling

BLUF

A modeling study conducted in the United Kingdom by the National Institute for Health Research (NIHR) utilized data from the COVID-19 outbreak in China and a country specific age-structured contact matrix to create two models to predict transmission in 151 countries. Using a reproductive ratio of 2.4 in China to fit their model, they estimate the reproductive ratio of other countries based off two hypotheses: transmission is independent of symptoms or transmission is dependent on symptoms (Figures 1 and 2). The models demonstrate that if transmission is highly dependent on symptom presentation, countries with older populations are likely to have the highest reproductive numbers, while if transmission is equally likely from symptomatic and asymptomatic cases, countries with younger populations will have the highest reproductive ratios.

ABSTRACT

The 2019-2020 pandemic of atypical pneumonia (COVID-19) caused by the virus SARS-CoV-2 has spread globally and has the potential to infect large numbers of people in every country. Estimating the country-specific basic reproductive ratio is a vital first step in public-health planning. The basic reproductive ratio (R_0) is determined by both the nature of pathogen and the network of human contacts through which the disease can spread, which is itself dependent on population age structure and household composition. Here we introduce a transmission model combining age-stratified contact frequencies with age-dependent susceptibility, probability of clinical symptoms, and transmission from asymptomatic (or mild) cases, which we use to estimate the country-specific basic reproductive ratio of COVID-19 for 152 countries. Using early outbreak data from China and a synthetic contact matrix, we estimate an age-stratified transmission structure which can then be extrapolated to 151 other countries for which synthetic contact matrices also exist. This defines a set of country-specific transmission structures from which we can calculate the basic reproductive ratio for each country. Our predicted R_0 is critically sensitive to the intensity of transmission from asymptomatic cases; with low asymptomatic transmission the highest values are predicted across Eastern Europe and Japan and the lowest across Africa, Central America and South-Western Asia. This pattern is largely driven by the ratio of children to older adults in each country and the observed propensity of clinical cases in the elderly. If asymptomatic cases have comparable transmission to detected cases, the pattern is reversed. Our results demonstrate the importance of age-specific heterogeneities going beyond contact structure to the spread of COVID-19. These heterogeneities give COVID-19 the capacity to spread particularly quickly in countries with older populations, and that intensive control measures are likely to be necessary to impede its progress in these countries.

FIGURES

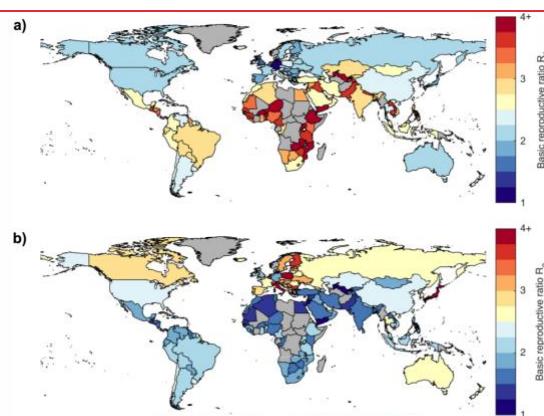


Fig 1. Basic reproductive ratio by country. (a) Estimated basic reproductive ratio for each country assuming contact structure only; (b) estimated basic reproductive ratio for each country based on China CDC case data [13]. Gray countries are those not included in Prem et al.'s study [13].

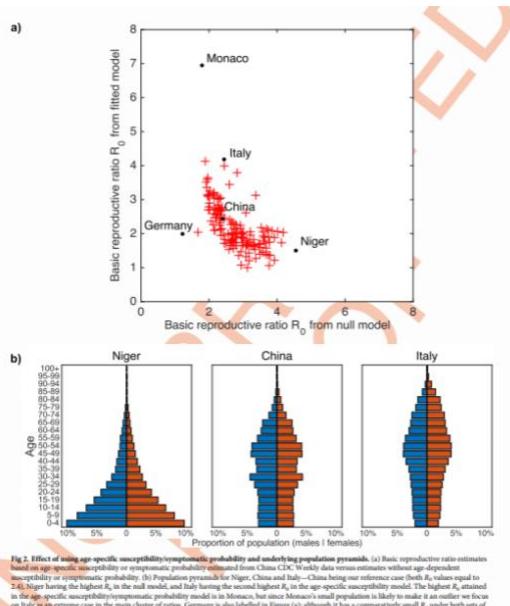


Fig 2. Effect of using age-specific susceptibility/susceptibility probability and underlying population pyramids. (a) Basic reproductive ratio estimates from fitted model vs null model for various countries. (b) Population pyramids for Niger, China and Italy—China being our reference case (both R_0 values equal to 2.4). Niger having the highest R_0 in the null model, and Italy having the second highest R_0 in the age-specific susceptibility model. The highest R_0 attained in the age-specific susceptibility model is 7.22 for Monaco in the fitted model, but Monaco's value is likely to increase to 7.22 based on the new data. The data points correspond to the main cluster of ratios. Germany is labeled in Figure (a) although it has a considerably small R_0 under both sets of assumptions, the proportional change from 1.22 in the null model to 1.99 based on the China CDC data is almost as dramatic as that seen for Italy (2.44 to 4.00). Data from [42].

PREDICTION OF THE TRANSITION FROM SUB-EXPONENTIAL TO THE EXPONENTIAL TRANSMISSION OF SARS-COV-2 AND EPIDEMIC NOWCASTING FOR METRO-ZONES: EXPERIENCES FROM CHENNAI-METRO-MERGE, INDIA

Krishnamurthy K, Ambikapathy B, Kumar A, Britto L.. JMIR Public Health Surveill. 2020 Jul 1. doi: 10.2196/21152. Online ahead of print.

Level of Evidence: Other - Modeling

BLUF

Epidemiologists created a model to predict the COVID-19 epidemic's transition from sub-exponential to exponential growth in Chennai, India (Figure 2). Based on case data from March 7-April 29, 2020, their model predicts the transition occurs eight weeks after the first case cluster (Figure 3). The data predicted the likelihood of transmission on public transit with maximum probability of infection in train coaches at 50% capacity [$P(0.2674)$] and single train coach [$P(0.3061)$]. The authors suggest their model provides evidence to support early public health responses in public transit to prevent the transition to exponential transmission in major metropolitan areas.

ABSTRACT

BACKGROUND: Several countries adopted lockdown to slowdown the exponential transmission of the COVID-19 epidemic. Disease transmission models and the epidemic forecasts at national level steer the policy to implement appropriate intervention strategies and budgeting. However, it is critical to design a data-driven reliable model for nowcasting for the small population, in particular metro cities. **OBJECTIVE:** The objective of this work is to analyze the transition of the epidemic from sub-exponential to exponential transmission in Chennai metro-zone and to analyze the probability of SARS-CoV-2 secondary infections while availing the public transport systems in the city. **METHODS:** A single geographical zone "Chennai-Metro-Merge" was constructed by combining Chennai district with three bordering districts. Sub-exponential and exponential models were developed to analyze and predict the progression of COVID-19 epidemic. Probabilistic models were applied to assess the probability of secondary infections while availing the public transport after the release of the lockdown. **RESULTS:** The model predicted that transition from sub-exponential to exponential transmission occurs around eighth week after the reporting a cluster of cases. The probability of the secondary infections with a single index case in an enclosure of the city bus and the sub-urban train general coach and ladies coach was found to be 0.192, 0.074 and 0.114 respectively. **CONCLUSIONS:** Nowcasting at the early stage of the epidemic predicts the probable time point of the exponential transmission and alerts the public health system. After the lockdown release, public transports will be the major sources of SARS-CoV-2 transmission in metro cities and appropriate strategies based on nowcasting are highly desirable. **CLINICALTRIAL:**

FIGURES

Constructed study site "Chennai-Metro-Merge" by combining Chennai district with three bordering districts Chengalpattu, Kanchipuram and Thiruvallur. The estimated total population of the constructed single geographical zone by 2020 is 15,208,505.



Figure 2. Constructed study site "Chennai-Metro-Merge" by combining Chennai district with three bordering districts Chengalpattu, Kanchipuram and Thiruvallur. The estimated total population of the constructed single geographical zone by 2020 is 15,208,505.

The reported number of COVID-19 cases (includes effect of intervention) and the output of the sub-exponential and the exponential models, shown as a function of time.

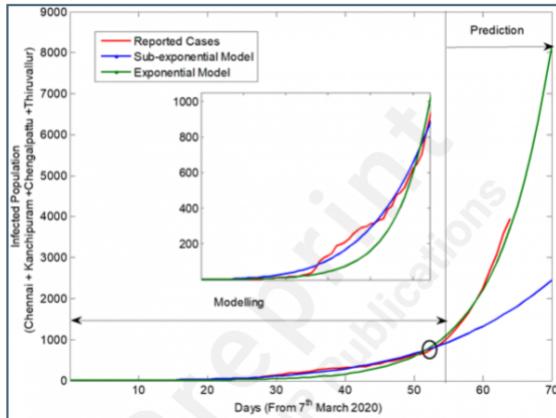


Figure 3. The reported number of COVID-19 cases (includes effect of intervention) and the output of the sub-exponential and the exponential models, shown as a function of time.

EXCESS DEATHS FROM COVID-19 AND OTHER CAUSES, MARCH-APRIL 2020

Woolf SH, Chapman DA, Sabo RT, Weinberger DM, Hill L.. JAMA. 2020 Jul 1. doi: 10.1001/jama.2020.11787. Online ahead of print.

Level of Evidence: Other - Modeling

BLUF

A modeling study conducted by Virginia Commonwealth University School of Medicine, from March 1 to April 25, 2020, found an excess of 87,001 (95% CI: 86,578-87,423) deaths in the United States (Table), 56,246 of which were a direct result of COVID-19, suggesting that the pandemic has resulted in massive extra casualties from what would be expected for this time period. Deaths from other underlying causes also increased during this time (Figure): heart disease (89%), cerebrovascular disease (35%), Alzheimer's disease (64%), and diabetes (96%), but additional studies are required to determine if these increased death rates represent societal disruptions due to the pandemic which impacted care or non-respiratory COVID-19 manifestations.

FIGURES

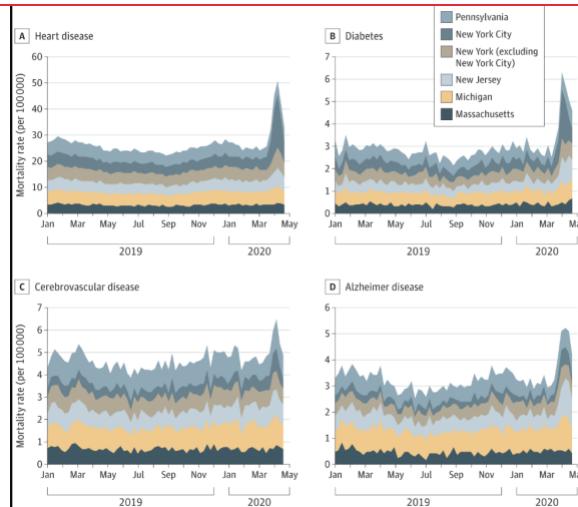


Figure. Weekly Death Rates From January 2019 Through April 2020. Data refer only to underlying causes of death; COVID-19 may have been a contributing cause in an unknown number of deaths. New Jersey and New York City experienced the largest relative increases

Table. Excess Deaths From March 1, 2020, to April 25, 2020, Attributed and Not Attributed to Coronavirus Disease 2019 (COVID-19)*								
Jurisdiction	Expected deaths, No. (95% CI) ^b	Observed deaths, No. (CI)	Excess deaths, No. (95% CI)	Covid-19 deaths ^c	Reported deaths, No.	Excess deaths, No. (95% CI)	Deaths not attributed to COVID-19 ^d	Excess deaths, No. (95% CI)
United States ^e	419,058 (418,636 to 419,481)	505,059	87,001 (86,578 to 87,423)	56,246	65	30,755 (\$0,332 to 31,177)	35	
Jurisdictions with highest COVID-19 death counts*								
New York City	8369 (8310 to 8427)	29,703	21,314 (21,276 to 21,735)	14,952	70	6,982 (6124 to 6441)	30	
New Jersey	11,458 (11,388 to 11,528)	23,174	11,715 (11,646 to 11,788)	8037	69	3,679 (3609 to 3749)	31	
New York (excluding New York City)	15,603 (15,519 to 15,686)	24,611	9,008 (8925 to 9090)	6569	73	2,439 (2356 to 2523)	27	
Michigan	15,217 (15,134 to 15,300)	20,232	5,015 (4932 to 5098)	3372	67	1,643 (1569 to 1726)	33	
Massachusetts	9316 (9253 to 9378)	13,412	4,096 (4034 to 4159)	3122	76	974 (912 to 1037)	24	
Pennsylvania	17,178 (17,089 to 17,268)	22,304	5,126 (5036 to 5215)	2752	54	2,374 (2288 to 2463)	46	
Other jurisdictions								
Illinois	16,559 (16,473 to 16,646)	20,310	3,751 (3,664 to 3,837)	2051	55	1,700 (1613 to 1786)	45	
California	42,253 (42,121 to 42,405)	46,289	4,026 (3884 to 4168)	1801	45	2,225 (2,083 to 2,367)	55	
Louisiana	7097 (7044 to 7150)	9082	1,985 (1932 to 2038)	1594	80	391 (338 to 444)	20	
Florida	33,550 (33,427 to 33,678)	35,766	2,216 (2088 to 2345)	1,750	56	968 (838 to 1095)	44	
Indiana	10,459 (10,391 to 10,525)	11,612	1,131 (1147 to 1280)	997	82	216 (150 to 283)	18	
Maryland	7664 (7608 to 7719)	9561	1,897 (1842 to 1953)	979	52	918 (863 to 974)	48	
Georgia	13,205 (13,128 to 13,281)	14,576	1,371 (1295 to 1448)	973	71	398 (322 to 475)	29	
Colorado	6,374 (6323 to 6424)	7573	1,199 (1149 to 1250)	822	69	377 (327 to 428)	31	
Texas	31,398 (31,277 to 31,520)	33,672	2,274 (2152 to 2395)	809	36	1,465 (1347 to 1586)	64	
Ohio	18,752 (18,660 to 18,844)	19,387	615 (543 to 727)	794	125	-159 (-251 to -67)	-25	
Washington	8849 (8789 to 8910)	9982	1,031 (972 to 1093)	719	70	314 (253 to 374)	30	
Virginia	10,679 (10,612 to 10,747)	12,045	1,366 (1298 to 1433)	526	39	840 (772 to 907)	61	
Arizona	9,777 (9713 to 9842)	10,734	957 (892 to 1021)	365	38	592 (527 to 656)	62	
Missouri	9985 (9920 to 10,050)	10,504	519 (454 to 584)	335	65	184 (119 to 249)	35	
Alabama	8079 (8022 to 8136)	8631	552 (495 to 609)	317	57	235 (178 to 292)	43	
Wisconsin	8448 (8380 to 8508)	9013	565 (505 to 675)	288	51	277 (217 to 331)	49	
Arkansas	4832 (4790 to 4873)	5403	571 (530 to 613)	252	44	319 (278 to 361)	56	
Rhode Island	1641 (1621 to 1661)	1870	229 (209 to 249)	250	109	-21 (-41 to -1)	-9	
Kentucky	7451 (7386 to 7505)	7621	170 (116 to 225)	215	126	-45 (-99 to 10)	-26	
South Carolina	7786 (7729 to 7842)	8561	775 (719 to 832)	213	27	562 (506 to 619)	73	
Nevada	4090 (4052 to 4127)	4328	238 (201 to 276)	213	89	25 (-1 to 63)	11	
Oklahoma	5824 (5777 to 5871)	6285	481 (414 to 508)	193	42	268 (221 to 315)	58	
District of Columbia	947 (934 to 960)	1223	276 (265 to 289)	185	67	91 (78 to 104)	33	
Tennessee	11,604 (11,534 to 11,675)	12,224	620 (549 to 690)	172	28	448 (377 to 518)	72	
Iowa	4741 (4699 to 4782)	4815	74 (31 to 116)	123	164	-48 (-89 to -6)	-64	
Oregon	5684 (5638 to 5731)	6101	417 (370 to 463)	114	27	303 (256 to 349)	73	
Delaware	1409 (1391 to 1427)	1623	214 (196 to 332)	113	53	101 (83 to 119)	47	
Kansas	4133 (4095 to 4170)	4254	121 (84 to 159)	104	86	17 (-20 to 55)	14	
New Mexico	2896 (2866 to 2926)	2969	73 (43 to 103)	89	121	-16 (-46 to 14)	-21	
West Virginia	1894 (1872 to 1916)	2044	150 (128 to 172)	61	41	89 (67 to 111)	59	
Nebraska	2615 (2587 to 2643)	2715	100 (72 to 128)	51	51	49 (21 to 77)	49	
Idaho	2202 (2117 to 2277)	2321	119 (94 to 144)	46	39	73 (48 to 98)	61	
Maine	2347 (2321 to 2373)	2368	21 (-5 to 47)	41	195	-20 (-46 to 6)	-95	
Arkansas	4973 (4930 to 5015)	5051	78 (33 to 123)	37	47	41 (-1 to 84)	53	
West Virginia	3335 (3300 to 3369)	3538	31 (13 to 38)	27	777	-24 (-58 to 11)	-677	
Utah	2952 (2921 to 2982)	3182	230 (200 to 464)	26	11	204 (174 to 235)	89	
Vermont	903 (890 to 916)	1018	115 (102 to 128)	11	10	104 (91 to 117)	90	
Wyoming	718 (708 to 729)	782	64 (53 to 74)	0	0	64 (53 to 74)	100	
South Dakota	1268 (1251 to 1284)	1305	38 (21 to 55)	0	0	38 (22 to 55)	100	
Montana	1614 (1594 to 1634)	1637	23 (13 to 43)	0	0	23 (3 to 43)	100	

*Data were collected from the National Center for Health Statistics with "negative" excess deaths (COVID-19 deaths subtracted from projected deaths), including Alaska (-45 deaths), Hawaii (-45 deaths), and North Dakota (-344 deaths).

^aUnderlying cause of death or a contributing cause.

^bThe US total was calculated as the sum of results for 48 states and the District of Columbia. Data for Connecticut and North Carolina were omitted because of delays in reporting.

^cSeasonal average predicted by regression model.

^dCOVID-19 deaths include deaths in which COVID-19 was identified as the

Table. Excess Deaths From March 1, 2020, to April 25, 2020, Attributed and Not Attributed to Coronavirus Disease 2019 (COVID-19)

SYMPTOMS AND CLINICAL PRESENTATION

REMOTE PSYCHOPHYSICAL EVALUATION OF OLFACTORY AND GUSTATORY FUNCTIONS IN EARLY-STAGE CORONAVIRUS DISEASE 2019 PATIENTS: THE BOLOGNA EXPERIENCE OF 300 CASES

Petrocelli M, Ruggiero F, Baietti AM, Pandolfi P, Salzano G, Salzano FA, Lechien JR, Saussez S, De Riu G, Vaira LA.. J Laryngol Otol. 2020 Jul 1:1-12. doi: 10.1017/S0022215120001358. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

Using an at home psychophysical test validated by Vaira et al (Table 4), this cohort study conducted at Bellaria-Maggiore Hospital in Bologna, Italy from April 16 to May 2, 2020 found that of the 300 SARS-CoV-2 positive patients, 70% had chemosensitive dysfunction (loss of smell, taste, or both). Gustatory dysfunction (Table 6) significantly correlated with fever ($OR=2.132$, 95% CI=1.299–3.499, $p=0.003$) and female gender ($OR=1.936$, 95% CI=1.139–3.386, $p = 0.014$) while olfactory dysfunction (Table 5) was not significantly associated with other symptoms. This study suggests that the proposed psychophysical test could be utilized to safely evaluate COVID-19 symptoms and that development of gustatory and olfactory dysfunction are associated with COVID-19.

FIGURES

Table 4. Chemosensory function assessment results

Parameter	Patients (n (%))
Chemosensory dysfunctions	
– Olfactory & taste disorders	164 (54.7)
– Only olfactory disorders	26 (8.7)
– Only taste disorders	20 (6.7)
– Total	210 (70)
– No taste or olfactory disorders	90 (30)
Olfactory dysfunctions	
– Anosmia	141 (47)
– Severe hyposmia	22 (7.3)
– Moderate hyposmia	19 (6.3)
– Mild hyposmia	8 (2.7)
– Normal	110 (36.7)
Gustatory dysfunctions	
– Ageusia	114 (38)
– Severe hypogeusia	22 (7.3)
– Moderate hypogeusia	30 (10)
– Mild hypogeusia	18 (6)
– Normal	116 (38.7)

Parameter	Olfactory dysfunction patients (n (%))	No olfactory dysfunction (n (%))	OR	95% CI for OR		Fisher's exact test value
				Lower limit	Upper limit	
^a Gender*olfactory dysfunction ^b						
- Female	149 (66.2)	76 (33.8)	1.626	0.955	2.768	0.073
- Male	41 (54.7)	34 (45.3)				
^a Age*olfactory dysfunction ^b						
- <50 years old	128 (65)	69 (35)	1.227	0.751	2.005	0.415
- ≥50 years old	62 (60.2)	41 (39.8)				
^a Fever*olfactory dysfunction ^b						
- Fever	136 (71.6)	54 (28.4)	1.556	0.946	2.558	0.082
- No fever	68 (61.8)	42 (38.2)				
^a Headache*olfactory dysfunction ^b						
- Headache	89 (66.9)	44 (33.1)	1.322	0.821	2.128	0.251
- No headache	101 (60.5)	66 (39.5)				
^a Pneumonia*olfactory dysfunction ^b						
- Pneumonia	52 (70.3)	22 (29.7)	1.507	0.856	2.654	0.155
- No pneumonia	138 (61.1)	88 (38.9)				

^aDependent variable; ^bindependent variable. OR = odds ratio; CI = confidence interval

Parameter	Gustatory dysfunction patients (n (%))	No gustatory dysfunction (n (%))	OR	95% CI for OR		Fisher's exact test value
				Lower limit	Upper limit	
^a Gender*gustatory dysfunction ^b						
- Female	147 (65.3)	78 (34.7)	1.936	1.139	3.286	0.014
- Male	37 (49.3)	38 (50.7)				
^a Age*gustatory dysfunction ^b						
- <50 years old	123 (62.4)	74 (37.6)	1.144	0.703	1.863	0.587
- ≥50 years old	61 (59.2)	42 (40.8)				
^a Fever*gustatory dysfunction ^b						
- Fever	137 (64.7)	67 (35.3)	2.132	1.299	3.499	0.003
- No fever	47 (49)	49 (51)				
^a Headache*gustatory dysfunction ^b						
- Headache	82 (61.6)	51 (38.4)	1.102	0.919	1.636	0.919
- No headache	102 (61.1)	65 (38.9)				
^a Pneumonia*gustatory dysfunction ^b						
- Pneumonia	48 (64.9)	26 (35.1)	1.222	0.707	2.11	0.473
- No pneumonia	136 (60.2)	90 (39.8)				

^aDependent variable; ^bindependent variable. OR = odds ratio; CI = confidence interval

POSITIVE SARS-COV-2 RNA RECURS REPEATEDLY IN A CASE RECOVERED FROM COVID-19: DYNAMIC RESULTS FROM 108 DAYS OF FOLLOW-UP

Liu F, Cai ZB, Huang JS, Yu WY, Niu HY, Zhang Y, Sui DM, Wang F, Xue LZ, Xu AF.. Pathog Dis. 2020 Jun 27:ftaa031. doi: 10.1093/femspd/ftaa031. Online ahead of print.

Level of Evidence: 5 - Case report

BLUF

A 35 year-old male patient who received care at Xixi Hospital of Hangzhou in China recovered from COVID-19 and subsequently presented with recurrent symptoms necessitating two additional hospitalizations over a 108 day observation period. The patient's hospitalizations are summarized in Figure 1 and lab findings over this time period are presented in Figure 2. These findings have potential implications on the possibility of recurrent COVID-19 disease and may also suggest a need for reassessment of the appropriateness of hospital discharge criteria and current quarantine protocols.

ABSTRACT

The evidence of long-term clinical dynamic on Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) RNA re-positive case are less. We performed a 108 days follow-up on dynamic clinical presentations in a case, who hospitalized three times due to the positive recurrence of SARS-CoV-2 RNA after discharge, to understand the prognosis of the 2019-Coronavirus disease (COVID-19). In this case, positive SARS-CoV-2 recurred even after apparent recovery (normal CT imaging, no clinical symptoms, negative SARS-CoV-2 on stool sample and negative serum IgM test) from COVID-19, viral shedding duration lasted for 65 days, the time from symptom onset to disappearance was up to 95 days. Erythrocyte-associated indicators, liver function and serum lipid metabolism presented abnormal throughout during the observation period. Awareness of atypical presentations such as this one is important to prompt the improvement of the management of COVID-19.

FIGURES

Fig. 1

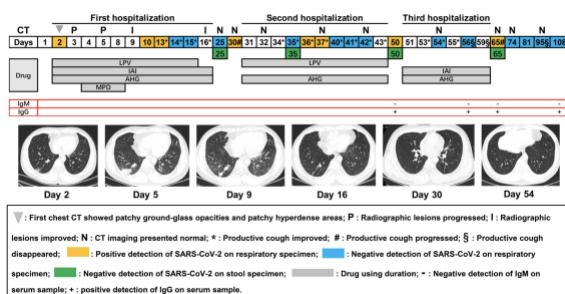


Figure 1. Time dynamics of virus, chest radiograph and clinical symptom on a case recovered from COVID-19 during the observation period. LPV: lopinavir; IAI: interferon α 2b atomization inhalation; AHG: arbidol hydrochloride granules; MPD: methylprednisolone.

Fig. 2

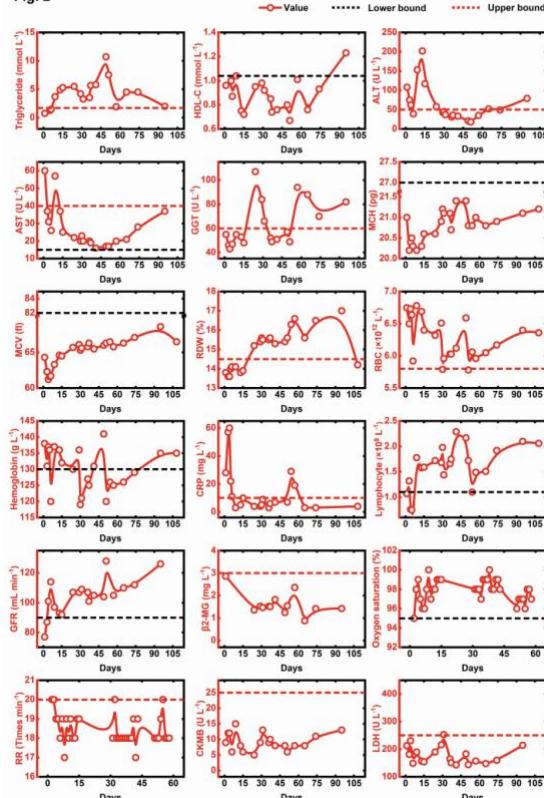


Figure 2. The temporal changes of laboratory indicators in a patient recovered from COVID-19. HDL-C: high-density lipoprotein cholesterol; ALT: alanine transaminase; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase; MCH: mean corpuscular hemoglobin; MCV: mean corpuscular volume; RDW: red cell distribution width; RBC: red blood cell count; CRP: rapid c-reactive protein; GFR: glomerular filtration rate; β 2-MG: β 2-macroglobulin; RR: respiratory rate; CKMB: creatine kinase isoenzyme; LDH: lactate dehydrogenase.

TREATMENT RECOMMENDATIONS FOR PERSISTENT SMELL AND TASTE DYSFUNCTION FOLLOWING COVID-19-THE COMING DELUGE

Levy JM.. JAMA Otolaryngol Head Neck Surg. 2020 Jul 2. doi: 10.1001/jamaoto.2020.1378. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

This study details how loss of smell and taste is a common symptom of COVID-19, with about 10% of affected patients having symptoms which persist longer than one month following initial diagnosis. Based on infection growth charts, providers can expect a considerable rise in patients seeking therapy for these symptoms, and currently the only efficacious and disease-specific treatment is olfactory training, in addition to some evidence supporting the use of topical corticosteroids. The authors

recommend building on these treatment guidelines while acknowledging the need for new research in this area as the quantity of patients experiencing persistent loss of taste and smell is expected to rise over the coming months.

ADULTS

CHARACTERISTICS OF ADULT OUTPATIENTS AND INPATIENTS WITH COVID-19 - 11 ACADEMIC MEDICAL CENTERS, UNITED STATES, MARCH-MAY 2020

Tenforde MW, Billig Rose E, Lindsell CJ, Shapiro NI, Files DC, Gibbs KW, Prekker ME, Steingrub JS, Smithline HA, Gong MN, Aboodi MS, Exline MC, Henning DJ, Wilson JG, Khan A, Qadir N, Stubblefield WB, Patel MM, Self WH, Feldstein LR; CDC COVID-19 Response Team.. MMWR Morb Mortal Wkly Rep. 2020 Jul 3;69(26):841-846. doi: 10.15585/mmwr.mm6926e3.
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

The CDC Influenza Vaccine Effectiveness in the Critically Ill (IVY) Network conducted a multi-state telephone survey between 15 April and 24 May 2020 of 350 adult (≥ 18 years) inpatients and outpatients at 11 United States academic medical centers who had a positive SARS-CoV-2 test (confirmed via reverse transcription-polymerase chain reaction [RT-PCR]). Authors found:

- Inpatients were older with more underlying chronic conditions (cardiovascular disease, respiratory disease, diabetes [$p < .001$]), less likely to be white ($p < .008$), and more likely to have an annual household income $< \$25,000$ ($p = .003$).
- Inpatients were also more likely to report dyspnea ($p < .001$) and fewer returned to baseline health after 14-21 days (39% versus 64%; $p = .001$).
- 46% of participants reported close contact with an individual who had COVID-19 before becoming infected (most commonly a family member [45%] or work colleague [34%]) and out of the 64% of participants who were employed, only 17% were able to telework.

The results provide epidemiological insight and suggest a need for increased screening, investigation, and contact tracing paired with social distancing and isolation measures to control community transmission and ensure workplace safety, especially given the frequent lack of a known contact.

ABSTRACT

Descriptions of coronavirus disease 2019 (COVID-19) in the United States have focused primarily on hospitalized patients. Reports documenting exposures to SARS-CoV-2, the virus that causes COVID-19, have generally been described within congregate settings, such as meat and poultry processing plants (1) and long-term care facilities (2). Understanding individual behaviors and demographic characteristics of patients with COVID-19 and risks for severe illness requiring hospitalization can inform efforts to reduce transmission. During April 15-May 24, 2020, telephone interviews were conducted with a random sample of adults aged ≥ 18 years who had positive reverse transcription-polymerase chain reaction (RT-PCR) test results for SARS-CoV-2 in outpatient and inpatient settings at 11 U.S. academic medical centers in nine states. Respondents were contacted 14-21 days after SARS-CoV-2 testing and asked about their demographic characteristics, underlying chronic conditions, symptoms experienced on the date of testing, and potential exposures to SARS-CoV-2 during the 2 weeks before illness onset (or the date of testing among those who did not report symptoms at the time of testing). Among 350 interviewed patients (271 [77%] outpatients and 79 [23%] inpatients), inpatients were older, more likely to be Hispanic and to report dyspnea than outpatients. Fewer inpatients (39%, 20 of 51) reported a return to baseline level of health at 14-21 days than did outpatients (64%, 150 of 233) ($p = 0.001$). Overall, approximately one half (46%) of patients reported known close contact with someone with COVID-19 during the preceding 2 weeks. This was most commonly a family member (45%) or a work colleague (34%). Approximately two thirds (64%, 212 of 333) of participants were employed; only 35 of 209 (17%) were able to telework. These findings highlight the need for screening, case investigation, contact tracing, and isolation of infected persons to control transmission of SARS-CoV-2 infection during periods of community transmission. The need for enhanced measures to ensure workplace safety, including ensuring social distancing and more widespread use of cloth face coverings, are warranted (3).

CLINICAL CHARACTERISTICS AND FACTORS ASSOCIATED WITH LONG-TERM VIRAL EXCRETION IN PATIENTS WITH SARS-COV-2 INFECTION: A SINGLE CENTER 28-DAY STUDY

BLUF

A retrospective, single-center study conducted in China between January 19 and February 17, 2020 found that 38 of 99 COVID-19 patients had prolonged SARS-CoV-2 positive test results; median 19 days. Additionally, patients with prolonged SARS-CoV-2 positive tests had greater disease severity; 52.6% admitted to the ICU versus 16.4% of those without prolonged disease course. Other independent risk factors for having a prolonged positive test included being male, immunoglobulin use, lymphocyte count, fecal viral RNA, and a high APACHE II score (Figure 1, Table 3). Based on these associations the authors suggest these risk factors may increase the odds of more severe COVID-19 infection.

ABSTRACT

BACKGROUND: Despite the ongoing spread of COVID-19, knowledge about factors affecting prolonged viral excretion is limited. **METHODS:** In this study, we retrospectively collected data from 99 hospitalized patients with COVID-19 between January 19 and February 17 in Zhejiang Province, China. We classified them into two groups based on whether the virus test results eventually became negative. Cox proportional hazards regression was used to evaluate factors associated with SARS-CoV-2 shedding. **RESULTS:** Among 99 patients, 61 patients had SARS-CoV-2 clearance (virus-negative group), but 38 patients had sustained positive results (virus-positive group). The median duration of SARS-CoV-2 excretion was 15 days (IQR 12-19) among the virus-negative patients. The shedding time was significantly increased if fecal SARS-CoV-2 RNA test results were positive. Male sex (HR, 0.58 [95% CI, 0.35-0.98]), immunoglobulin use (HR, 0.42 [95% CI, 0.24-0.76]), APACHE II score (HR, 0.89 [95% CI, 0.84-0.96]), and lymphocyte count (HR, 1.81 [95% CI, 1.05-3.1]) were independent factors associated with a prolonged duration of SARS-CoV-2 shedding. Antiviral therapy and corticosteroid treatment were not independent factors. **CONCLUSIONS:** SARS-CoV-2 RNA clearance time was associated with sex, disease severity and lymphocyte function. The current antiviral protocol and low-to-moderate dosage of corticosteroid had little effect on the duration of viral excretion.

FIGURES

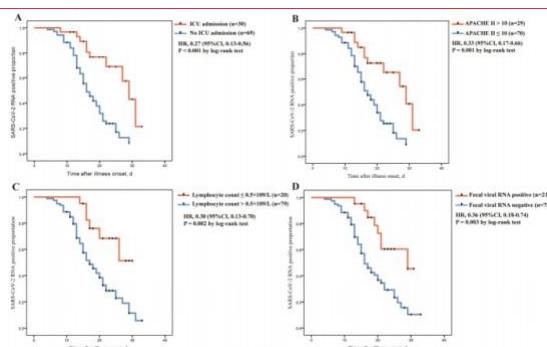


Figure 1. A, Cumulative proportion of patients with detectable SARS-CoV-2 RNA among patients who were transferred to ICU and those who were in general ward by day after illness onset. B, Cumulative proportion of patients with detectable SARS-CoV-2 RNA among those whose APACHE II score ≥ 10 and those whose APACHE II score ≤ 10 by day after illness onset. C, Cumulative proportion of patients with detectable SARS-CoV-2 RNA among those whose lymphocyte count $\leq 0.5 \times 10^9/L$ and those whose lymphocyte count $\geq 0.5 \times 10^9/L$ by day after illness onset. D, Cumulative proportion of patients with detectable SARS-CoV-2 RNA among those with positive fecal viral RNA and those with negative fecal viral RNA by day after illness onset.

Age	0.99 (0.97-1.00)	0.067	0.99 (0.97-1.00)	0.098
Male sex	0.56 (0.34-0.94)	0.029	0.58 (0.35-0.98)	0.042
Current smoking	0.98 (0.46-2.07)	0.982	1.48 (0.65-3.35)	0.345
Hypertension	0.58 (0.33-1.02)	0.058	0.63 (0.26-1.10)	0.104
Diabetes	0.87 (0.41-1.82)	0.865	1.18 (0.53-2.62)	0.680
Days from illness onset to ARV start	0.96 (0.90-1.02)	0.221	0.95 (0.89-1.01)	0.105
Two ARV combination therapy	0.72 (0.38-1.39)	0.331	0.90 (0.45-1.81)	0.899
Corticosteroid treatment	0.85 (0.46-1.57)	0.599	1.00 (0.53-1.89)	0.990
Days from illness onset to corticosteroid start	0.94 (0.87-1.02)	0.127	0.94 (0.86-1.02)	0.121
Immunoglobulin use	0.38 (0.22-0.66)	0.001	0.42 (0.24-0.76)	0.004
Days from illness onset to immunoglobulin start	0.91 (0.81-1.03)	0.136	0.93 (0.82-1.05)	0.231
Antibiotic treatment	0.61 (0.37-1.03)	0.614	0.70 (0.42-1.19)	0.187
APACHE II score	0.89 (0.85-0.95)	0.000	0.89 (0.84-0.96)	0.002
Lymphocyte count	1.86 (1.16-2.99)	0.010	1.81 (1.05-3.10)	0.033

Table 3. Multivariable Analyses of Factors Associated With Duration of SARS-COV-2 RNA Detection in 99 Hospitalized Patients.

SMOKING PREVALENCE AND COVID-19 IN EUROPE

Tsigaris P, Teixeira da Silva JA. Nicotine Tob Res. 2020 Jul 1:ntaa121. doi: 10.1093/ntr/ntaa121. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

This ecological study discusses the prevalence of smoking, COVID-19 cases, and mortality in 38 European nations (27 were members of the European Union; 19 Eurozone) through May 30, 2020, and found a negative association between prevalence of smoking and COVID-19 cases in the 38 European nations ($p<0.0001$; 95% CI [-0.756, -0.313])(Figure 1). Furthermore, there was no direct association between smoking prevalence and COVID-19 mortality ($p=0.6260$). The researchers acknowledge these results are limited by the data on smoking prevalence in hospitalized cases, however, they recommend further studies to better understand the effects of smoking on COVID-19.

ABSTRACT

INTRODUCTION: This ecological study investigates the association between smoking prevalence and COVID-19 occurrence and mortality in 38 European nations as of 30th May 2020. **METHODS:** Data were collected from Our World in Data. Regression analysis was conducted to adjust for potential confounding factors such as economic activity (GDP), the rate of COVID-19 testing, and the stringency of COVID-19 control policies. **RESULTS:** There was a statistically significant negative association between smoking prevalence and the prevalence of COVID-19 across the 38 European nations after controlling for confounding factors ($p = 0.001$). A strong association was found between the prevalence of COVID-19 per million people and economic activity ($p = 0.002$) and the rate of COVID-19 testing ($p = 0.0006$). Nations with stricter policy enactment showed fewer COVID-19 cases per million people, but the association was not significant ($p = 0.122$). Delaying policy enactment was associated with a greater prevalence of COVID-19 ($p = 0.0535$). Evidence of a direct association between smoking prevalence and COVID-19 mortality was not found ($p = 0.626$). There was a strong positive association between COVID-19 mortality rate and the prevalence of COVID-19 cases ($p < 0.0001$) as well as the proportion of the population over 65 years of age ($p = 0.0034$) and a negative association with the rate of COVID-19 testing ($p = 0.0023$). **CONCLUSIONS:** We found a negative association between smoking prevalence and COVID-19 occurrence at the population level in 38 European countries. This association may not imply a true or causal relationship, and smoking is not advocated as a prevention or treatment of COVID-19.

FIGURES

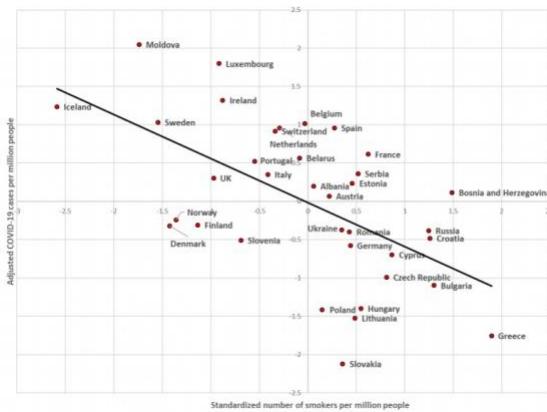


Figure 1 Number of smokers versus COVID-19 cases in European nations. All variables were transformed to natural logarithms. COVID-19 cases per million people was adjusted for the influence of other confounding factors and standardized against standardized number of smokers per million people. The partial correlation coefficient is -0.576 ($p < 0.001$) with a 95% CI $[-0.761, -0.306]$, very similar to the simple Pearson correlation coefficient -0.575 ($p < 0.001$) with a 95% CI $[-0.756, -0.313]$, indicating that the confounding factors controlled for did not distort the simple linear association that had been detected, either because these confounding factors are uncorrelated with the smoking prevalence rate or have an offsetting impact on the COVID-19 prevalence when the smoking rate was correlated with the confounding factors. Smoking prevalence was negatively correlated with the rate of COVID-19 testing but was positively correlated with Max SI.

BRIEF REPORT: ANTI-PHOSPHOLIPID ANTIBODIES IN CRITICALLY ILL PATIENTS WITH CORONAVIRUS DISEASE 2019 (COVID-19)

Xiao M, Zhang Y, Zhang S, Qin X, Xia P, Cao W, Jiang W, Chen H, Ding X, Zhao H, Zhang H, Wang C, Zhao J, Sun X, Tian R, Wu W, Wu D, Ma J, Chen Y, Zhang D, Xie J, Yan X, Zhou X, Liu Z, Wang J, Du B, Qin Y, Gao P, Lu M, Hou X, Wu X, Zhu H, Xu Y, Zhang W, Li T, Zhang F, Zhao Y, Li Y, Zhang S. *Arthritis Rheumatol*. 2020 Jun 30. doi: 10.1002/art.41425. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

This cross-sectional study conducted at the Peking Union Medical College Hospital in Wuhan, China evaluated serum samples from 79 patients with COVID-19 and found antiphospholipid antibodies (aPLs) to be elevated in 47% of critically ill patients with COVID-19, the most common of which was an IgA isotype, suggesting the involvement of pulmonary and intestinal mucosa in the disease process (Table 2). Elevated aPLs were not found in non-critically ill patients. These findings may help in the identification of COVID-19 patients at risk of thrombotic events.

ABSTRACT

OBJECTIVES: Coagulopathy is one of the characteristics of critically ill patients with Coronavirus Disease 2019 (COVID-19). Antiphospholipid antibodies (aPLs) contribute to coagulopathy, but their role in COVID-19 remains unclear. We aimed to determine the prevalence and characteristics of aPLs in patients with COVID-19. **METHODS:** Sera collected from 66 critically ill and 13 non-critically ill patients with COVID-19 were tested for anti-cardiolipin (aCL) and anti-beta2-glycoprotein 1 (abeta2GP1) (IgG, IgM, and IgA) and IgG abeta2GP1-D1 by the chemiluminescence assay (CIA) and IgM and IgG anti-phosphatidylserine/prothrombin (aPS/PT) by ELISA. **RESULTS:** aPLs were detected in 47.0% of critically ill patients (31/66), but not in patients with non-critical conditions. IgA abeta2GP1 was the most common aPL, present in 28.8% (19/66) critically ill patients, followed by IgG aCL (25.8%, 17/66) and IgG abeta2GP1 (18.2%, 12/66). For multiple aPLs, IgA abeta2GP1+IgA aCL was the most common type (22.7%, 15/66), followed by IgA abeta2GP1+IgG aCL+ IgG abeta2GP1 (15.2%, 10/66). aPLs emerge around 35-39 days post-disease onset. Dynamic analysis of aPLs revealed 4 patterns based on persistence or transient appearance of the aPLs. Patients with multiple aPLs displayed significantly higher incidence of cerebral infarction ($p=0.023$). **CONCLUSIONS:** aPLs were common in critically ill patients. Multiple medium or high levels aPLs may help identify patients at risk of developing cerebral infarction. aPLs may be transient and disappear within a few weeks, but in genetically predisposed patients, COVID-19 may trigger the development of "COVID-19-induced-APS-like-syndrome". Long-term follow-up on COVID-19 patients positive for aPLs would be of great importance.

FIGURES

Table 2. Prevalence and characteristics of aPLs in patients with COVID-19

Antiphospholipid antibodies (aPLs)	Critically-ill (n=66)	Non-Critically-ill (n=13)
Overall prevalence in any aPLs, n (%)	31 (47.0)	0
IgA aCL, n (%)	17 (25.8)	0
IgG aCL, n (%)	4 (6.0)	0
IgM aCL, n (%)	2 (3.0)	0
Lupus anticoagulant, n (%)	2 (3.0)	0
IgA a β 2GP1, n (%)	19 (28.8)	0
IgG a β 2GP1, n (%)	12 (18.2)	0
IgM a β 2GP1, n (%)	1 (1.5)	0
IgG a β 2GP1-D1, n (%)	2 (3.0)	0
IgM aPS/PT, n (%)	7 (10.6)	0
IgG aPS/PT, n (%)	0	0
IgA aCL+IgA a β 2GP1, n (%)	15 (22.7)	0
IgM aCL+IgM a β 2GP1, n (%)	1 (1.5)	0
IgA a β 2GP1+IgG a β 2GP1, n (%)	1 (1.5)	0
LA+IgA aCL+IgA a β 2GP1, n (%)	1 (1.5)	0
IgA aCL+IgA a β 2GP1+IgG a β 2GP1, n (%)	10 (15.2)	0
IgA aCL+IgG a β 2GP1+IgM aCL, n (%)	1 (1.5)	0
IgA aCL+IgA a β 2GP1+IgM aPS/PT, n (%)	1 (1.5)	0
IgA aCL+IgG aCL+IgA a β 2GP1+ IgG a β 2GP1, n (%)	4 (6.1)	0
LA+IgA aCL+IgG aCL+IgA a β 2GP1+ IgG a β 2GP1, n (%)	1 (1.5)	0

The cutoff values for positivity in all aPLs except IgM/IgG aPT/PS were set >20 U based on the recommendations of the manufacturer. The cutoff values for positivity in IgM/IgG aPT/PS were set >30 U based on the recommendations by the manufacturer. a β 2GP1, anti- β 2-glycoprotein 1 antibodies; a β 2GP1-D1, anti- β 2-glycoprotein domain 1 antibodies; aCL, anticardiolipin antibodies; aPS/PT, anti-phosphatidylserine/prothrombin, LA, lupus anticoagulants; N/D, not determined

OLFACtORY AND GUSTATORY OUTCOMES IN COVID-19: A PROSPECTIVE EVALUATION IN NONHOSPITALIZED SUBJECTS

Paderno A, Mattavelli D, Rampinelli V, Grammatica A, Raffetti E, Tomasoni M, Gualtieri T, Taboni S, Zorzi S, Del Bon F, Lombardi D, Deganello A, Redaelli De Zinis LO, Schreiber A.. Otolaryngol Head Neck Surg. 2020 Jun 30:194599820939538.

doi: 10.1177/0194599820939538. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

A prospective cohort study conducted in Northern Italy analyzed the rate and timing of recovery of olfactory (OD) and gustatory (GD) dysfunction in 151/213 completed online surveys from COVID-19 patients from April 27-May 5, 2020 (see summary for results). They found high rates of OD/GD resolution within the first month of symptom onset but suggest additional investigations are warranted to better characterize different patterns of presentation and resolution.

SUMMARY

The data revealed 83% had OD and 89% presented with GD and the breakdown of each as follow:

1. OD - 26% partial OD, 76% anosmia.
2. GD - 30% partial GD, 70% ageusia
3. OD (87%) had higher recovery rates than GD (82%) in the first month after symptom onset (Table 3).
4. 10%-15% had incomplete resolution even after 45 days.
5. 2% had recurrence after complete resolution of symptoms. Negative nasopharyngeal swab results were observed before the recurrence.
6. Late recovery of symptoms depended on 3 variables - grade of dysfunction (partial/total), gender (female p=0.013), and the presence of nasal congestion (p=0.046).
7. Nasal congestion led to the longer recovery of OD and no influence on GD noted. (Figure 1 and 2).

ABSTRACT

OBJECTIVE: To prospectively assess the rate and timing of recovery of olfactory (OD) and gustatory (GD) dysfunction in patients affected by COVID-19. **STUDY DESIGN:** Cohort study. **SETTING:** Population-based evaluation in a COVID-19 high-prevalence region. **SUBJECTS AND METHODS:** We analyzed the clinical course of OD and GD in a cohort of home-quarantined SARS-CoV-2-positive patients from Northern Italy. Physicians administered a survey-based questionnaire at recruitment (T0). During follow-up, patients responded to online dedicated surveys modulated according to symptoms at T0. **RESULTS:** A total of 151 patients completed the follow-up survey. OD and/or GD were observed in 83% and 89% of subjects, respectively. Resolution rates of OD and GD at 30 days from onset were 87% and 82%, respectively. Risk factors for late resolution were grade of dysfunction at onset (total vs partial), gender, and presence of nasal congestion. Three (2%) patients previously reporting complete resolution of symptoms complained of subsequent recurrence of OD and/or GD after a mean of 19 days

from resolution of the previous episode. CONCLUSION: COVID-19-related OD and GD had high rate of resolution in the first month from onset of symptoms. However, in 10% to 15% of patients, these symptoms showed only partial improvement after this period.

FIGURES

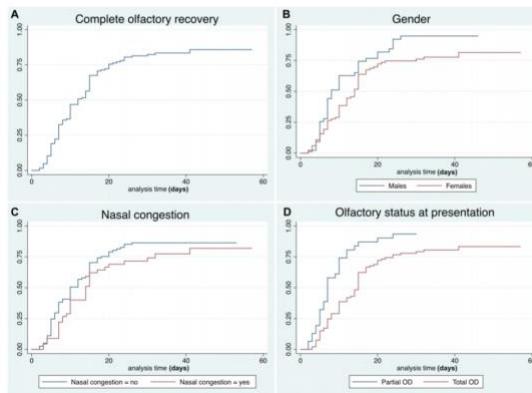


Figure 1: Kaplan-Meier curves showing the recovery pattern of olfactory dysfunction in the entire series (A), according to gender (B), nasal congestion (C), and grade of olfactory dysfunction at presentation (D).

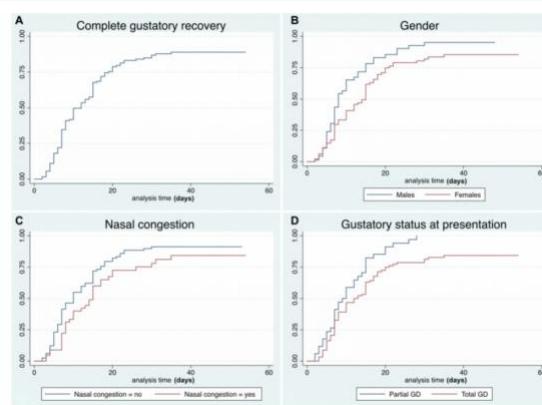


Figure 2: Kaplan-Meier curves showing the recovery pattern of gustatory dysfunction in the entire series (A), according to gender (B), nasal congestion (C), and grade of gustatory dysfunction at presentation (D).

Table 3. Multivariable Analysis of Factors Associated With Timing of Recovery of Olfactory and Gustatory Dysfunction.^a

Variable	Hazard ratio	P value	95% CI
Olfactory dysfunction			
Gender	0.74	.147	0.49-1.12
Grade of dysfunction	0.43	<.001	0.27-0.68
Nasal congestion	0.59	.016	0.38-0.90
Gustatory dysfunction			
Gender	0.66	.040	0.44-0.98
Grade of dysfunction	0.68	.083	0.44-1.05
Nasal congestion	0.73	.131	0.48-1.10

^aGender: male versus female; grade of dysfunction: partial versus total; nasal congestion: no versus yes.

Figure 2: Kaplan-Meier curves showing the recovery pattern of gustatory dysfunction in the entire series (A), according to gender (B), nasal congestion (C), and grade of gustatory dysfunction at presentation (D).

RISK OF ISCHEMIC STROKE IN PATIENTS WITH CORONAVIRUS DISEASE 2019 (COVID-19) VS PATIENTS WITH INFLUENZA

Merkler AE, Parikh NS, Mir S, Gupta A, Kamel H, Lin E, Lantos J, Schenck EJ, Goyal P, Bruce SS, Kahan J, Lansdale KN, LeMoss NM, Murthy SB, Stieg PE, Fink ME, Iadecola C, Segal AZ, Cusick M, Campion TR Jr, Diaz I, Zhang C, Navi BB.. JAMA Neurol. 2020 Jul 2. doi: 10.1001/jamaneurol.2020.2730. Online ahead of print.
Level of Evidence: 4 - Cohort study or control arm of randomized trial

BLUF

This retrospective cohort study using COVID-19 patient data at 2 academic hospitals in New York City from March 4 through May 2, 2020 ($n = 1916$), found that COVID-19 patients were more likely to have an acute ischemic stroke than influenza A/B patients from January 1, 2016 to May 31, 2018 ($n = 1486$) (odds ratio, 7.6; 95% CI, 2.3-25.2). Although COVID-19 patients are mostly older males with underlying co-morbidities and presenting with a stronger inflammatory response, the authors recommend further investigation to determine the role these factors may play in stroke evolution. They advocate for doctors to be more vigilant in the early diagnosis and treatment of stroke in patients with COVID-19.

ABSTRACT

Importance: It is uncertain whether coronavirus disease 2019 (COVID-19) is associated with a higher risk of ischemic stroke than would be expected from a viral respiratory infection. **Objective:** To compare the rate of ischemic stroke between patients with COVID-19 and patients with influenza, a respiratory viral illness previously associated with stroke. **Design, Setting, and Participants:** This retrospective cohort study was conducted at 2 academic hospitals in New York City, New York, and included adult patients with emergency department visits or hospitalizations with COVID-19 from March 4, 2020, through May 2, 2020. The comparison cohort included adults with emergency department visits or hospitalizations with influenza A/B from January 1, 2016, through May 31, 2018 (spanning moderate and severe influenza seasons). **Exposures:** COVID-19 infection confirmed by evidence of severe acute respiratory syndrome coronavirus 2 in the nasopharynx by polymerase chain reaction and laboratory-confirmed influenza A/B. **Main Outcomes and Measures:** A panel of neurologists adjudicated the primary outcome of acute ischemic stroke and its clinical characteristics, mechanisms, and outcomes. We used logistic regression to compare the proportion of patients with COVID-19 with ischemic stroke vs the proportion among patients with influenza. **Results:** Among 1916 patients with emergency department visits or hospitalizations with COVID-19, 31 (1.6%; 95% CI, 1.1%-2.3%) had an acute ischemic stroke. The median age of patients with stroke was 69 years (interquartile range, 66-78 years); 18 (58%) were men. Stroke was the reason for hospital presentation in 8 cases (26%). In comparison, 3 of 1486 patients with influenza (0.2%; 95% CI, 0.0%-0.6%) had an acute ischemic stroke. After adjustment for age, sex, and race, the likelihood of stroke was higher with COVID-19 infection than with influenza infection (odds ratio, 7.6; 95% CI, 2.3-25.2). The association persisted across sensitivity analyses adjusting for vascular risk factors, viral symptomatology, and intensive care unit admission. **Conclusions and Relevance:** In this retrospective cohort study from 2 New York City academic hospitals, approximately 1.6% of adults with COVID-19 who visited the emergency department or were hospitalized experienced ischemic stroke, a higher rate of stroke compared with a cohort of patients with influenza. Additional studies are needed to confirm these findings and to investigate possible thrombotic mechanisms associated with COVID-19.

UNDERSTANDING THE PATHOLOGY

COVID-19 SEVERITY CORRELATES WITH WEAKER T CELL IMMUNITY, HYPERCYTOKINEMIA AND LUNG EPITHELIUM INJURY

Wang Z, Yang X, Zhou Y, Sun J, Liu X, Zhang J, Mei X, Zhong J, Zhao J, Ran P.. Am J Respir Crit Care Med. 2020 Jul 1. doi: 10.1164/rccm.202005-1701LE. Online ahead of print.

Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

An experimental study of six severely ill and six recovering COVID-19 patients conducted at The First Affiliated Hospital at Guangzhou Medical University in Guangzhou, China during a three month period found that:

1. Increased CD4+ and CD8+ T cell populations typically correlated with higher severity of COVID-19 disease (Figure 1),
2. Levels of sydecan-1 and interleukin-6 (IL-6) were significantly higher in the severe group than the recovered group (Figure 1), and
3. Increased neutralizing antibodies correlated with COVID-19 disease remission (Figure 1), suggesting the mechanisms of immune function need to be better elucidated in order to understand the pathogenesis of SARS-CoV-2.

FIGURES

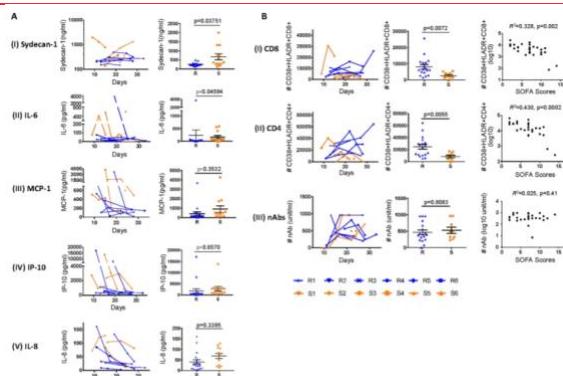


Figure 1. S = severe, R = regressed(A) (Left panel) The levels of representative lung injury and inflammation effectors in the blood plasma of the R and S groups of COVID-19 patients at different days after disease onset. (Right panel) Comparison of the levels of sydecan-1, IL-6, MCP-1, IP-10 and IL-8. The data are presented as the mean \pm SEM (18 measurements from the 6 patients in R group and 12 measurements from the 6 patients in S group). Since the data contain multiple measurements over a time-period from individual patients, a linear mixed-effect model which is commonly applied for this kind of data analysis (9, 10) was used to determine if the mean level of a biomarker was statistically distinct between the R and S groups. Two linear mixed-effect models, one of which included the classification of R and S groups as a predictor, were fitted with each biomarker dataset and a likelihood ratio test was then performed to examine if the former model was acceptable. This was based on a confidence level of 95%, i.e., a p value less than 0.05 suggests that the mean biomarker level is statistically distinct between the R and S groups. The details of the statistical method, the data and the R code are publicly available at (https://github.com/wzhf1218/COVID19-Wang_et.al.git).

(B) (Left panel) The presence of CD38+HLA-DR+CD8+ T cells (I), CD38+HLA-DR+CD4+ T cells (II) and nAbs (III) in the blood plasma of the R and S groups of the COVID-19 patients at different timepoints. (Middle panel) Comparison of absolute numbers of CD38+HLA-DR+CD8+ T cells (I),

CD38+HLA-DR+CD4+ T cells (II) and nAbs (III) in 1 ml blood samples. The data are presented as the mean \pm SEM (18 measurements from the 6 patients in R group and 9 measurements from the 5 patients excluding patient S6 in S group) and the p values were calculated using the aforementioned statistical method. (Right panel) Correlation analyses between immune effectors (CD38+HLA-DR+ double positive CD8+/CD4+ T cells and nAb titers) and COVID-19 disease severity evaluated by imaging scores and oxygenation index (SOFA score) was carried out using the Linear Regression model.

INSIGHTS INTO PATHOGENESIS OF FATAL COVID-19 PNEUMONIA FROM HISTOPATHOLOGY WITH IMMUNOHISTOCHEMICAL AND VIRAL RNA STUDIES

Level of Evidence: 4 - Case-series

BLUF

Postmortem immunohistochemistry (IHC) and SARS-CoV-2 viral RNA detection by next generation sequencing (NGS) were performed on eight patients with COVID-19 diagnosed by real-time RT-PCR who presented with diffuse alveolar damage (DAD) (Table 1). Investigators found that in the acute phase of DAD, 1) viral antigen and RNA were present, 2) IHC staining was seen in pneumocytes, alveolar macrophages, and hyaline membranes, and 3) neutrophil infiltration was prominent. This is in contrast to organizing DAD, where 1) viral antigen and RNA were lost, 2) IHC staining was absent, and 3) chronic inflammatory cells rather than neutrophils were found (Table 2, Figure 2). These findings suggest that the role of SARS-CoV-2 and actions of a patient's immune system change throughout the course of DAD, and this knowledge could aid in constructing a more targeted treatment course in the future.

ABSTRACT

INTRODUCTION: We describe postmortem pulmonary histopathologic findings of COVID-19 pneumonia in patients with a spectrum of disease course, from rapid demise to prolonged hospitalization. **METHODS:** Histopathologic findings in postmortem lung tissue from eight patients who died from COVID-19 pneumonia were reviewed. Immunohistochemistry (IHC) and next generation sequencing (NGS) were performed to detect virus. **RESULTS:** Diffuse alveolar damage (DAD) was seen in all cases with a spectrum of acute phase and/or organizing phase. IHC with monoclonal antibodies against SARS-CoV-2 viral nucleoprotein and spike protein detected virus in areas of acute but not organizing DAD, with intracellular viral antigen and RNA expression seen predominantly in patients with duration of illness less than 10 days. Major vascular findings included thrombi in medium and large caliber vessels, platelet microthrombi detected by CD61 IHC, and fibrin microthrombi. **CONCLUSIONS:** Presence of SARS-CoV-2 viral RNA by NGS early in the disease course and expression of viral antigen by IHC exclusively in the acute but not in the organizing phase of DAD, suggests that the virus may play a major role in initiating the acute lung injury of DAD, but when DAD progresses to the organizing phase, the virus may have been cleared from the lung by the patient's immune response. These findings suggest the possibility of a major change during the disease course of COVID-19 pneumonia that may have therapeutic implications. Frequent thrombi and microthrombi may also present potential targets for therapeutic intervention.

FIGURES

Patient	*Duration from onset of symptoms to death (days)	*Mechanical ventilation resuscitation	Attempted resuscitation	Phase of DAD	Interstitial inflammation ^b	Airway changes	Vascular changes ^c	Infect present
1	7	No	Yes	Acute	Neutrophils (ADAD)	Marked acute bronchitis and bronchiolitis; aspiration pneumonia	Acute vascular inflammation in areas of acute pneumonia; mild chronic venular inflammation; platelet microthrombi	No
2	3	No	Yes	Acute	Neutrophils (ADAD)	Mild acute bronchitis and bronchiolitis	Platelet microthrombi	No
3	9	Yes (2)	Yes	Acute and organizing	Lymphocytes (OADD) and Neutrophils (ADAD)	Mild acute bronchitis and bronchiolitis; focal chronic bronchiolitis	Medium-sized arterial thrombi; fibrin and platelet microthrombi; mild chronic venular inflammation	No
4	13	Yes (3)	Yes	Acute and organizing	Lymphocytes (OADD) and neutrophils (ADAD)	Mild acute bronchitis and bronchiolitis; mild focal chronic bronchiolitis	Platelet microthrombi	No
5	16	Yes (>1)	No	Organizing and acute	Lymphocytes (OADD) and eosinophils	Mild acute bronchitis and bronchiolitis	Medium sized arterial thrombi; platelet	Yes
6	20	Yes (11)*	No	Organizing	[focal] neutrophils (ADAD)		microthrombi; mild chronic venular inflammation	
7	25	Yes (9)	No	Organizing and acute (focal)	Lymphocytes (OADD) and neutrophils (ADAD)	Mild chronic bronchitis and bronchiolitis	Large arterial thrombus; Platelet microthrombi	No
8	17	Yes (<1)	No	Organizing and acute (focal)	Lymphocytes (OADD) and neutrophils (ADAD)	Mild acute and chronic bronchitis; mucosal plugging in proximal bronchi	Large and medium sized arterial thrombi; fibrin and platelet microthrombi; mild chronic venular inflammation	No

Abbreviations: ADAD, acute phase of DAD; DAD, diffuse alveolar damage; OADD, organizing phase of DAD

*Patient was intubated twice, initially for 10 days, then off for 4 days before reintubated for 1 day.

^bThe neutrophils were seen focally in areas of acute DAD and the lymphocytes in areas of organizing DAD.

^cVascular changes seen on histologic examination of H&E-stained slides without assistance of immunohistochemistry include thrombi, fibrin microthrombi and vasculitis. Platelet microthrombi by CD61 immunohistochemistry were seen in all cases.

*Clinical and limited pulmonary pathology data for patients 1-5, 7 and 8 will be published in *EClinicalMedicine* (20).

Table 1. Disease course and histopathological findings in autopsy of lung tissue from patients who died from COVID-19 pneumonia.

Case	Onset to death (days)	Viral RNA*	Anti-SARS-CoV spike protein (clone 1A9)		Anti-SARS-CoV nucleoprotein (clone 001)		Histologic findings in FFPE tissue used for NGS
			Acute DAD	Organizing DAD	Acute DAD	Organizing DAD	
1	7	Detected	++	NA	++	NA	Acute DAD
2	3	Detected	++	NA	++	NA	Acute DAD
3	9	Detected	+	-	+	-	Predominantly organizing DAD
4	13	Not detected	+*	NA	+	NA	DAD with focal acute DAD
5	16	Not detected	+*	NA	+	NA	Predominantly organizing DAD with focal acute DAD
6	20	Not detected	NA	-	NA	-	Organizing DAD
7	25	Not detected	NA*	NA*	NA*	NA*	Necrotizing pneumonia
8	17	Not detected	+*	-	+	-	Organizing DAD with very focal acute DAD

Table 2. Viral detection by next generation sequencing and immunohistochemistry and corresponding histology.

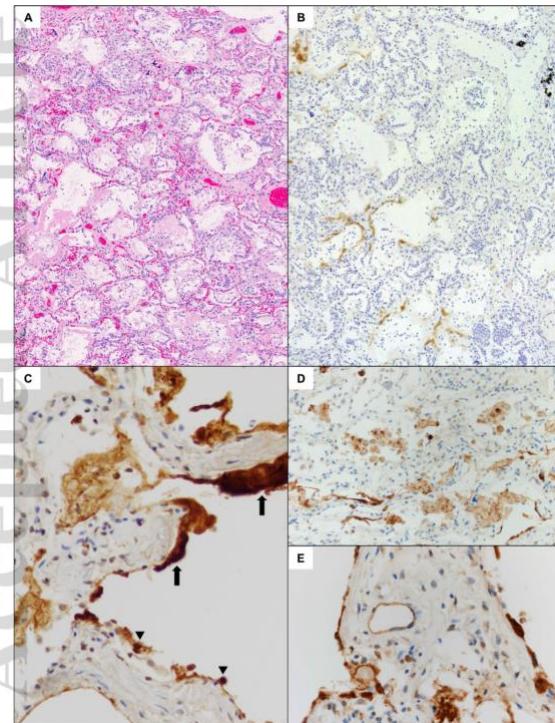


Table 2. Viral detection by next generation sequencing and immunohistochemistry and corresponding histology.

COVID-19 MEETS CYSTIC FIBROSIS: FOR BETTER OR WORSE?

Peckham D, McDermott MF, Savic S, Mehta A.. Genes Immun. 2020 Jul 1. doi: 10.1038/s41435-020-0103-y. Online ahead of print.

Level of Evidence: Other - Review / Literature Review

BLUF

A literature review by authors affiliated with the University of Leeds and University of Dundee (UK) found that cystic fibrosis (CF) patients with COVID-19 experienced less severe symptoms than would be expected. Although limited literature is available on this subject, the authors propose that this "protective effect" may be due to CF-altered cellular processes (i.e. autophagy, mitophagy, etc.) that may be critical to SARS-CoV-2 viral replication (Figure 1). Based on their review, the authors suggest further research in this area, especially into the role of the CF conductance regulator protein (CFTR) in COVID-19 pathogenesis for possible therapeutic targets and propose clinical trials to explore CF drugs in COVID-19 patients.

ABSTRACT

Cystic fibrosis (CF) is one of the most common autosomal recessive life-limiting conditions affecting Caucasians. The resulting defect in the cystic fibrosis transmembrane conductance regulator protein (CFTR) results in defective chloride and bicarbonate secretion, as well as dysregulation of epithelial sodium channels (ENaC). These changes bring about defective mucociliary clearance, reduced airway surface liquid and an exaggerated proinflammatory response driven, in part, by

infection. In this short article we explore the overlap in the pathophysiology of CF and COVID-19 infection and discuss how understanding the interaction between both diseases may shed light on future treatments.

FIGURES

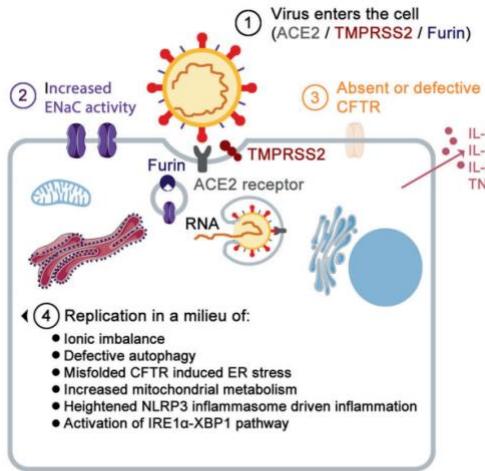


Fig. 1 SARS-CoV-2 and cystic fibrosis. The spike protein on the virion binds to the ACE2 cell membrane protein. Cellular entry is facilitated by the TMPRSS2 and furin enzymes, one or more of which may be altered in CF. Once inside the cell, viral processing, may be influenced either by overactive inflammation and/or CF-affected cellular processes including autophagy, mitophagy, endosomal function and cellular metabolism, which may all be co-opted by COVID-19 for viral replication.

DATA, REAGENTS, ASSAYS AND MERITS OF PROTEOMICS FOR SARS-COV-2 RESEARCH AND TESTING

Zecha J, Lee CY, Bayer FP, Meng C, Grass V, Zerweck J, Schnatbaum K, Michler T, Pichlmair A, Ludwig C, Kuster B.. Mol Cell Proteomics. 2020 Jun 26:mcp.RA120.002164. doi: 10.1074/mcp.RA120.002164. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

BLUF

A study conducted in Germany assessing the use of mass spectrometry-based proteomics in SARS-CoV-2 research, via development of a parallel reaction monitoring (PRM) assay and evaluating it by comparing SARS-CoV-2 positive cell lines to negative controls, found widespread proteome expression changes upon infection. The authors believe their results illustrate the potential for clinical use of proteomics in COVID-19 management.

SUMMARY

A study conducted in Germany presents high-quality liquid chromatography-mass spectrometry (LC-MS/MS) data on the proteomes of Vero E6, Calu-3, Caco-2, and ACE2-A549 cell lines, among others, in 54 SARS-CoV-2 positive and 37 negative samples. It was observed that viral interactomes varied among cell types:

- Vero E6 and ACE2-A549 cells were most susceptible to SARS-CoV-2 GFP-reporter virus.

- Caco-2 cells demonstrated lower infectability and Calu-3 cells showed no infection (Fig. 2C).

The study also presented a “physical and spectral library of 98 stable isotope-labeled, synthetic peptides representing 11 viral proteins along with optimized parallel reaction monitoring (PRM) assays that were tested on two diagnostic cohorts of in total 91 COVID-19 suspected individuals.” Their results revealed:

- Although ACE2 and TMPRSS2 co-expression in cells is an important factor for pathogenicity in olfactory epithelium, they are not found in the lungs despite the severity of disease in this area.

- There was a down regulation of proteins responsible for innate immunity such as GBP1 and MASP1 at high viral loads, which was not observed with lower viral loads.

- As anticipated, 24 hours after infection, viral protein expression increased substantially and could be detected by proteomics (Fig. 3A).

- Five of twenty-four COVID-19 PCR-positive cases were also positive by PRM on LC-MS/MS system (Fig. 5C), and all PCR-negative cases were also negative by PRM.

Although large population testing for COVID-19 will continue to rely on PCR-based detection, the authors believe the results of this study reveal potential for proteomics to have a clinical role in therapeutic stratification of COVID-19 patients as well as monitoring recovery.

ABSTRACT

As the SARS-CoV-2 pandemic continues to spread, thousands of scientists around the globe have changed research direction to understand better how the virus works and to find out how it may be tackled. The number of manuscripts on preprint servers is soaring and peer-reviewed publications using mass spectrometry-based proteomics are beginning to emerge. To facilitate proteomic research on SARS-CoV-2, this report presents deep-scale proteomes (10,000 proteins; >130,000 peptides) of common cell line models, notably Vero E6, Calu-3, Caco-2, and ACE2-A549 that characterize their protein expression profiles including viral entry factors such as ACE2 or TMPRSS2. Using the 9 kDa protein SRP9 and the breast cancer oncogene BRCA1 as examples, we show how the proteome expression data can be used to refine the annotation of protein-coding regions of the African green monkey and the Vero cell line genomes. Monitoring changes of the proteome upon viral infection revealed widespread expression changes including transcriptional regulators, protease inhibitors, and proteins involved in innate immunity. Based on a library of 98 stable-isotope labeled synthetic peptides representing 11 SARS-CoV-2 proteins, we developed PRM (parallel reaction monitoring) assays for nano-flow and micro-flow LC-MS/MS. We assessed the merits of these PRM assays using supernatants of virus-infected Vero E6 cells and challenged the assays by analyzing two diagnostic cohorts of 24 (+30) SARS-CoV-2 positive and 28 (+9) negative cases. In light of the results obtained and including recent publications or manuscripts on preprint servers, we critically discuss the merits of mass spectrometry-based proteomics for SARS-CoV-2 research and testing.

FIGURES

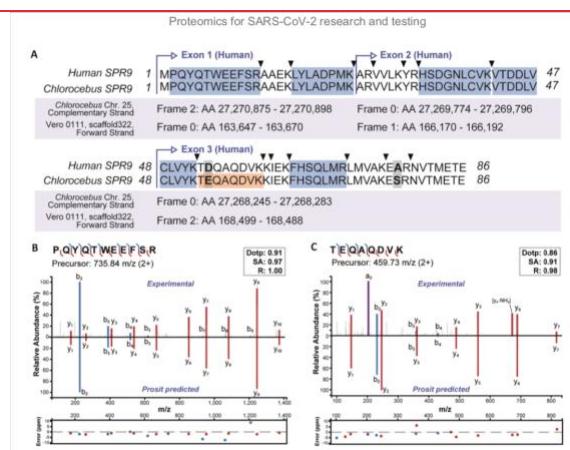


Figure 2. Proteomics-guided annotation of a missed gene in the Chlorocebus genome. (A) Alignment of the human SRP9 protein sequence with its Chlorocebus ortholog constructed from a six-frame translation of the genomic Chlorocebus and Vero JCRB0111 (Vero 0111) sequences. Peptides in blue map to all, the human, the Chlorocebus, and the Vero JCRB0111 sequences.

The peptide coloured in orange is unique for Chlorocebus and Vero JCRB0111 and was only identified in a refined search including the newly annotated monkey SRP9 sequence. Triangles indicate trypsin cleavage sites and bold-face letters mark amino acid differences between the sequences. (B) Mirror and m/z deviation plots of the experimental spectrum and the Prosit predicted spectrum for the N-terminal peptide of the human and Chlorocebus protein sequence. The similarity of the two spectra is measured by the dot product (dotp), the spectral contrast angle (SA) and the Pearson correlation coefficient (R) of the two spectra. (C) Same as in (B) but for the peptide that is unique for the Chlorocebus and Vero JCRB0111 sequences of SRP9.

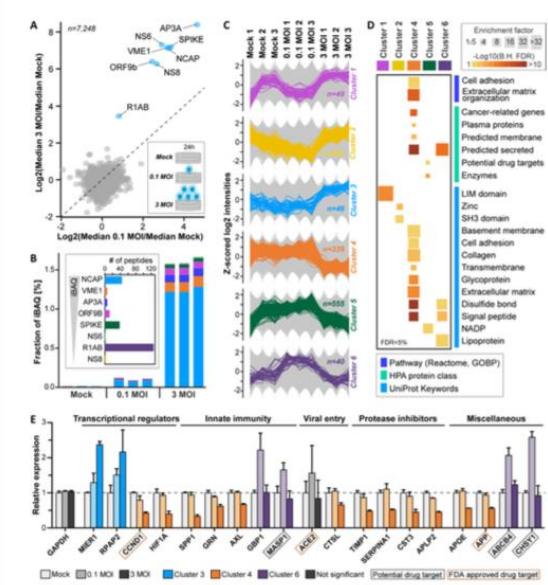


Figure 3. Vero E6 proteome response after infection with SARS-CoV-2. Vero E6 cells were infected with SARS-CoV-2 at 0.1 MOI, 3 MOI and mock in triplicate and proteomes were profiled 24h post infection. (A) Protein expression changes for 3 MOI vs. 0.1 MOI. Annotated viral proteins are marked in blue. (B) Bar chart showing the fractional abundance of viral proteins in the host cell proteome. The inset displays the number of identified peptides per virus protein ordered by decreasing cellular abundance. (C) Line charts illustrating the expression patterns of proteins in the six main clusters extracted from significantly regulated proteins. Background proteins are displayed in grey. (D) Functional categories enriched in clusters determined by Fisher's exact tests (B.H. FDR: Benjamini-Hochberg false discovery rate). (E) Examples for regulated proteins from different clusters. The dotted line indicates no change (exemplified by GAPDH).

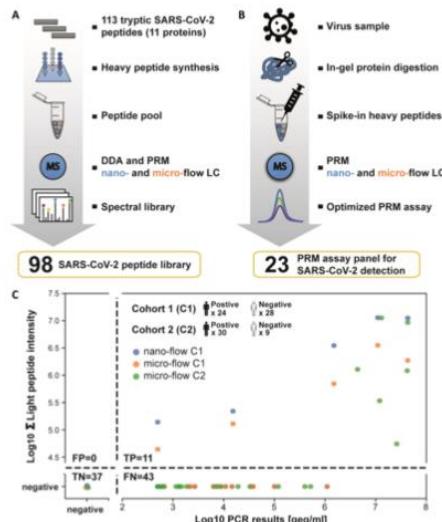


Figure 3. Vero E6 proteome response after infection with SARS-CoV-2. Vero E6 cells were infected with SARS-CoV-2 at 0.1 MOI, 3 MOI and mock in triplicate and proteomes were profiled 24h post infection. (A) Protein expression changes for 3 MOI vs. 0.1 MOI. Annotated viral proteins are marked in blue. (B) Bar chart showing the fractional abundance of viral proteins in the host cell proteome. The inset displays the number of identified peptides per virus protein ordered by decreasing cellular abundance. (C) Line charts illustrating the expression patterns of proteins in the six main clusters extracted from significantly regulated proteins. Background proteins are displayed in grey. (D) Functional categories enriched in clusters determined by Fisher's exact tests (B.H. FDR: Benjamini-Hochberg false discovery rate). (E) Examples for regulated proteins from different clusters. The dotted line indicates no change (exemplified by GAPDH).

UNRAVELING THE MYSTERY OF COVID-19 CYTOKINE STORM: FROM SKIN TO ORGAN SYSTEMS

BLUF

In this literature review, experts from India report that in addition to the involvement of respiratory, circulatory, neurological, and gastrointestinal systems, skin lesions may also be seen over the COVID-19 disease course (Figure 1). The authors suggest that improving cellular immunity at the initial phase of illness, depressing humoral response, and preventing hypoxicemic and reperfusion injuries may significantly reduce the morbidity and mortality of COVID-19.

SUMMARY

The authors' recommendations for COVID-19 treatment options are summarized below:

- Prevent disease: sanitization, wearing masks, social distancing, adopting a healthy balanced diet with anti-oxidants, getting sun exposure and adequate physical activity
- Counter initial pathogenesis: antiviral drugs (i.e. Remdesivir, oseltavir), chloroquine and hydroxychloroquine may be effective; moxifloxacin and macrolides may be used to avoid superadded bacterial infections
- Improve cell-mediated immunity: Mw vaccine (primarily used for leprosy), BCG vaccine (primarily used for tuberculosis), and other immunomodulators (i.e. vitamin D) may be effective in diverting and controlling the cytokine storm; clinical trials should assess the efficacy of these options against COVID-19
- Curb overactive humoral response: use of anti-inflammatory drugs (i.e. steroids) only for a short duration may be effective; immunosuppressants (i.e. mycophenolate, mofetil, tacrolimus, cyclosporin) may be effective if supported by clinical trials; some inflammatory cytokines inhibitors are under trial and may be effective treatments
- Mitigate hypoxicemic injury: vasodilators and judicious use of anticoagulants to prevent and/or treat microthrombi formation

ABSTRACT

COVID-19 is a global pandemic that emerged from Wuhan, China. Besides pneumonia and acute respiratory distress syndrome, the disease leads to multisystem involvement in the form of myocarditis, arrhythmias, cardiac arrest, gastrointestinal symptoms, hypoxicemic brain injury, acute liver and renal function impairment. There are also reports of cutaneous lesions in form of urticarial and maculopapular rashes, chilblain like fingers and toes (covid feet), livedoid vasculopathy and chicken-pox like or varicelliform vesicles. Clinically, many of these skin lesions are likely secondary to occlusion of small to medium blood vessels due to microthrombi formation or due to viral laden antigen-antibody immune complexes; and same explanation may hold true for possible hypoxicemic injury simultaneously occurring in other vital organs like lungs, heart, brain and kidneys. The histopathology, immunofluorescence and RT-PCR analysis of skin biopsies can provide useful insights for ascertaining the pathogenesis of this complex viral syndrome. Apparently, it is interplay of disarmed cellular immunity and over-activated humoral immunity that culminates in end-organ changes. The morbidity and mortality can be significantly reduced by upgrading the cellular immunity and downgrading the humoral response; along with prevention of hypoxicemic and reperfusion injuries by using antivirals, immunomodulators, antioxidants, anti-platelets and anticoagulants in judicious and phased manner. This article is protected by copyright. All rights reserved.

FIGURES

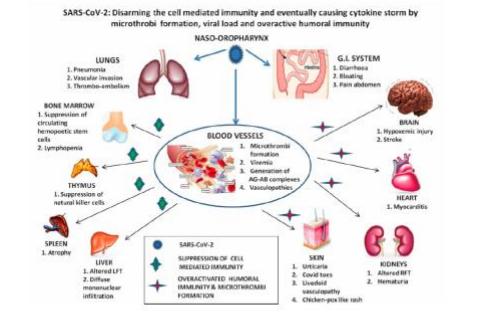


Figure 1: Flowchart explaining how the SARS-CoV-2 virus attacks the nasopharynx and gains entry into lung, gastrointestinal system and blood vessels due to abundant presence of ACE2 receptors. Cell mediated immunity is disarmed by atrophy and destruction of lymph nodes, thymus, spleen and liver. Blood vessels in lung are easy target due to presence of ACE2 receptors initiating cascade of micro-thrombi formation, immune complex deposition and exaggerated humoral immune response leading to subsequent hypoxicemic injury to various vital organs.

IN VITRO

INFECTABILITY OF HUMAN BRAINSPHERE NEURONS SUGGESTS NEUROTROPISM OF SARS-COV-2

Bullen CK, Hogberg HT, Bahadirli-Talbott A, Bishai WR, Hartung T, Keuthan C, Looney MM, Pekosz A, Romero JC, Sillé FCM, Um P, Smirnova L.. ALTEX. 2020 Jun 26. doi: 10.14573/altex.2006111. Online ahead of print.

Level of Evidence: 3 - Mechanism-based reasoning

BLUF

Through in-vitro experiments and the use of BrainSpheres, researchers at Johns Hopkins University detected expression of the angiotensin converting enzyme-2 receptor in neuronal cells, demonstrated the presence of SARS-CoV-2 in neural cells, and found increased levels of viral copies in neural cell lysate 72 hours post infection (Figures 2-3). This highlights the potential for devastating and long-lasting neurological effects due to SARS-CoV-2 infection of the nervous system.

ABSTRACT

Reports from Wuhan suggest that 36% of COVID-19 patients show neurological symptoms, and cases of viral encephalitis have been reported, suggesting that the virus is neurotropic under unknown circumstances. This is well established for other coronaviruses. In order to understand why some patients develop such symptoms and others do not, we address herein the infectability of the central nervous system (CNS). Reports that the ACE2 receptor - critical for virus entry into lung cells - is found in different neurons supports this expectation. We employ a human induced pluripotent stem cell (iPSC)-derived BrainSphere model, which we used earlier for Zika, Dengue, HIV and John Cunningham virus infection studies. We detected the expression of the ACE2 receptor but not TMPRSS2 in the model. Incubating the BrainSpheres for 6 hours with SARS-CoV-2 at multiplicity of infection (MOI) of 0.1 led to the infection of a fraction of neural cells with replication of the virus evident 72 hours later. Virus particles were found in the neuronal cell body extending into apparent neurite structures. PCR measurements corroborated the replication of the virus, suggesting at least a tenfold increase in virus copies per total RNA. Leveraging state-of-the-art 3D organotypic cell culture, which has been shown to allow both virus infection and (developmental) neurotoxicity but is at the same time simple enough to be transferred and used in a BSL-3 environment, we demonstrate, for the first time, the potential critically important neurotropism of SARS-CoV-2.

FIGURES

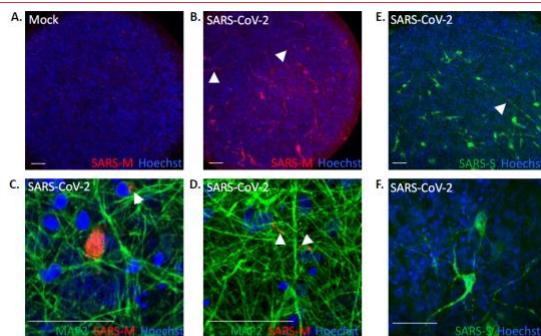
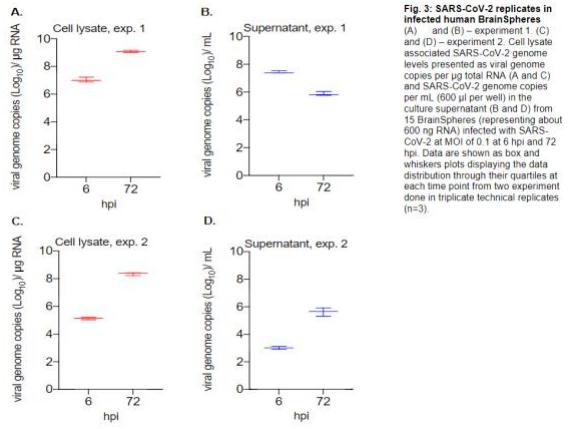


Fig. 2: A small fraction of neuronal cells in BrainSpheres contains virus particles at 72 hpi
BrainSpheres infected with SARS-CoV-2 at MOI of 0.1 were analyzed at 72 hpi for M protein (red) expression by immunofluorescence (A). A monoclonal antibody against SARS-CoV-2 spike protein was used to detect the neurons. Arrowheads indicate colocalization and presence of the virus in neurons (E) and (F) BrainSpheres stained for SARS-CoV-2 spike protein (green). Images are representative of five BrainSpheres. Nuclei are stained with Hoechst 33342 (blue). Scale bar 50 µm.



PHENOTYPE AND KINETICS OF SARS-COV-2-SPECIFIC T CELLS IN COVID-19 PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME

Weiskopf D, Schmitz KS, Raadsen MP, Grifoni A, Okba NMA, Endeman H, van den Akker JPC, Molenkamp R, Koopmans MPG, van Gorp ECM, Haagmans BL, de Swart RL, Sette A, de Vries RD.. Sci Immunol. 2020 Jun 26;5(48):eabd2071. doi: 10.1126/sciimmunol.abd2071.

Level of Evidence: Other - Mechanism-based reasoning

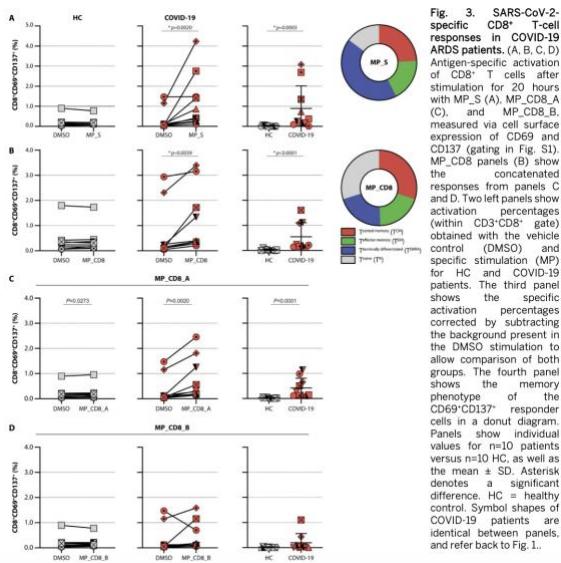
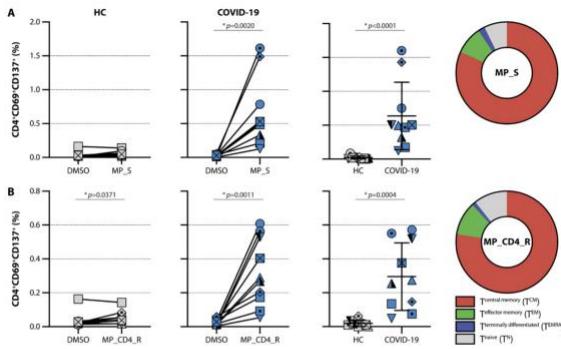
BLUF

In this study, a group of researchers evaluate the response of SARS-CoV-2 specific T cells through analysis of longitudinal peripheral blood mononuclear cells (PBMC) samples from 10 COVID-19 patients with acute respiratory distress syndrome who were admitted to the intensive care unit. They found that SARS-CoV-2 specific CD4+ and CD8+ T cells were detected in most patients within 2 weeks of infection (Figures 2 and 3), and cytokine profiles demonstrate that Th1 and effector cytokines dominated the response (Figure 5). The strongest responses were to the spike glycoprotein, which is consistent with previous studies. These findings are valuable to the development of an effective vaccine for the virus.

ABSTRACT

SARS-CoV-2 has been identified as the causative agent of a global outbreak of respiratory tract disease (COVID-19). In some patients the infection results in moderate to severe acute respiratory distress syndrome (ARDS), requiring invasive mechanical ventilation. High serum levels of IL-6, IL-10 and an immune hyperresponsiveness referred to as a 'cytokine storm' have been associated with poor clinical outcome. Despite the large numbers of COVID-19 cases and deaths, information on the phenotype and kinetics of SARS-CoV-2-specific T cells is limited. Here, we studied 10 COVID-19 patients who required admission to an intensive care unit and detected SARS-CoV-2-specific CD4+ and CD8+ T cells in 10 out of 10 and 8 out of 10 patients, respectively. We also detected low levels of SARS-CoV-2-reactive T cells in 2 out of 10 healthy controls not previously exposed to SARS-CoV-2, which is indicative of cross-reactivity due to past infection with 'common cold' coronaviruses. The strongest T-cell responses were directed to the spike (S) surface glycoprotein, and SARS-CoV-2-specific T cells predominantly produced effector and Th1 cytokines, although Th2 and Th17 cytokines were also detected. Furthermore, we studied T-cell kinetics and showed that SARS-CoV-2-specific T cells are present relatively early and increase over time. Collectively, these data shed light on the potential variations in T-cell responses as a function of disease severity, an issue that is key to understanding the potential role of immunopathology in the disease, and also inform vaccine design and evaluation.

FIGURES



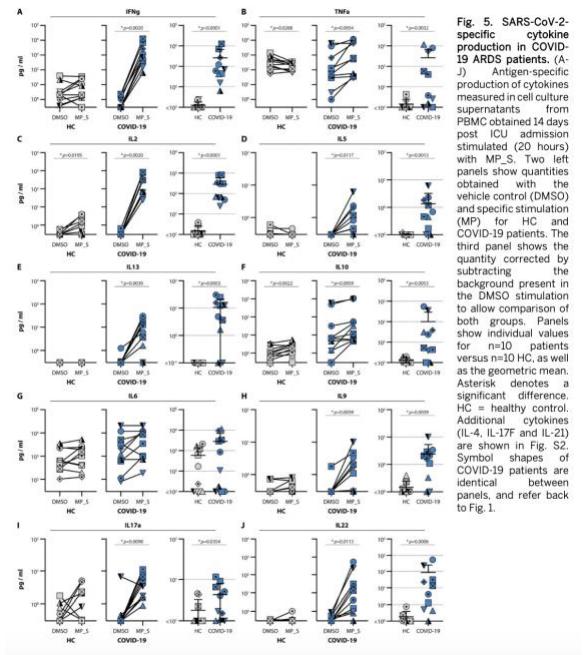


Fig. 5. SARS-CoV-2-specific cytokine production in COVID-19 ARDS patients. (A-J) Cytokine production of cytokines measured in cell culture supernatants from PBMC obtained 14 days post ICU admission stimulated (20 hours) with MP_S. Two left panels show raw data obtained with the vehicle control (DMSO) and specific stimulation (MP) for HC and COVID-19 patients. The third panel shows the quantity corrected by subtracting the background present in the DMSO stimulation to allow comparison of both groups. Panels show individual values for n=10 patients versus n=10 HC, as well as the geometric mean. Asterisk denotes a significant difference. HC = healthy control. Additional cytokines (IL-4, IL-17F and IL-21) are shown in Fig. S2. Symbol shapes of COVID-19 patients are identical between panels, and refer back to Fig. 1.

TRANSMISSION & PREVENTION

DEVELOPMENTS IN TRANSMISSION & PREVENTION

SARS-COV-2 VACCINES: 'WARP SPEED' NEEDS MIND MELDS NOT WARPED MINDS

Moore JP, Klasse PJ.. J Virol. 2020 Jun 26:JVI.01083-20. doi: 10.1128/JVI.01083-20. Online ahead of print.

Level of Evidence: Other - Review / Literature Review

BLUF

SUMMARY

Summary of additional review findings below:

- General concerns in vaccine development: Studies showed that immune responses to COVID-19 vaccines may enhance infection or exacerbate disease in individuals who become infected despite vaccination, which could result in public backlash against vaccines. Time lost during a spreading pandemic is another fundamental concern.
- Antibody responses in COVID-19 cases vary greatly during the clinical course: Extreme variation in antibody titers holds true across multiple cohort studies and may reflect pathological consequences of infection or be a result of samples collected too early in the disease course before their peak. Additionally, identifying what titers protect against disease in COVID-19 cohorts is difficult.
- Neutralizing monoclonal antibodies (nMAbs) to the SARS-CoV-2 S-protein: Strong sequence similarities among antibodies from different donors has useful implications for the response to S-protein vaccines on a population basis. The similarity of the receptor binding domain (RBD) epitopes for these nMAbs and their very limited maturation from germline sequences are encouraging indicators that potent polyclonal neutralizing antibodies (NAb) will be triggered by S-protein or RBD vaccines.
- Immunogenicity of SARS-CoV-2 vaccine candidates: Most industry-based vaccine programs fell into one of three general categories including nucleic-acid (mRNA or DNA) plasmids, replicating virus vectors (adenovirus or vaccinia virus) and recombinant S-proteins or the RBD. Collective needs are creating unusually aggressive timelines for a product that can be used widely in humans. Data suggests most rapidly produced vaccines (i.e. nucleic acids and virus vectors) may also be the least capable of eliciting high titers of antibodies and NAb to the S-protein (Figure 2).
- Vaccine challenge experiments in monkey models: A chimpanzee adenovirus construct (ChAdOx1 nCoV-19) vaccine was not a strong inducer of antibody responses to the S-protein in macaque animal models, which appeared true of DNA plasmids as well (Figure 2). Few macaques were completely protected from infection but a reduction in the severity of the already mild disease was noted.
- Protective antibody titer for a SARS-CoV-2 vaccine and length of persistence: Magnitude of antibody response to protect humans from SARS-CoV-2 infection and how long any protective response might last both remain unknown. Induction of B-cell memory responses to protect from disease may be more feasible, though booster immunizations could be necessary.
- Vaccine-mediated adverse events: Creating herd immunity against SARS-CoV-2 may require a vaccine efficacy rate of ~70%. Vaccinating during a pandemic could involve induction of weak and potentially deleterious priming responses in people who then encounter the virus before they receive their boosting immunizations, but given the unusual circumstances of the COVID-19 pandemic there is limited time for critical analysis of adverse events.
- Outcome scenarios: Favorably, efficacy trials will show that SARS-CoV-2 vaccines confer robust protection that will bring a prompt end to the pandemic. While feasible, it is not certain that vaccines rapidly manufactured in large volume (e.g., mRNA, DNA, adenovirus vectors) will be sufficiently immunogenic to elicit protective NAb responses in a high proportion of the population. Unfavorably, the first vaccines tested are not immunogenic enough to be protective but are not associated with significant adverse events before or after SARS-CoV-2 infection.

ABSTRACT

In this review, we address issues that relate to the rapid "Warp Speed" development of vaccines to counter the COVID-19 pandemic. We review the antibody response that is triggered by SARS-CoV-2 infection of humans, and how it may inform vaccine research. The isolation and properties of neutralizing monoclonal antibodies from COVID-19 patients provide additional information on what vaccines should try to elicit. The nature and longevity of the antibody response to coronaviruses are relevant to the potency and duration of vaccine-induced immunity. We summarize the immunogenicity of leading vaccine candidates tested to date in animals and humans, and discuss the outcome and interpretation of virus-challenge experiments in animals. By far the most immunogenic vaccine candidates for antibody responses are recombinant proteins, which are not included in the initial wave of "Warp Speed" immunogens. A substantial concern for SARS-CoV-2

vaccines is adverse events, which we review by considering what was seen in studies of SARS-CoV-1 and MERS-CoV vaccines. We conclude by outlining the possible outcomes of the "Warp Speed" vaccine program, which range from the hoped-for rapid success to a catastrophic adverse influence on vaccine uptake generally.

FIGURES

Table 1. Categories of vaccines for protection against SARS-CoV-2 infection and/or disease

Vaccine category	Safety ²	Speed and ease of production	Logistics of global distribution	Potential for NAb induction	Potential for cell-mediated immunity ³
Live attenuated virus	Substantial concerns	N/A ⁴	N/A	Probably high	Probably Good
Inactivated virus	Some concerns ⁵	Intermediate	Feasible	Moderate	Poor
Non-replicating virus vector (recombinant DNA virus)	High	High	Feasible	Weak	Probably good
DNA plasmid given by electroporation	High	High	Some concerns ⁶	Very weak	Probably good
mRNA	High	High	May be difficult ⁷	Weak	Probably good
Soluble or nanoparticle S- or RBD-protein, with adjuvant	High	Low ⁸	Feasible	High	Poor

Table 1 Footnotes:

- 1) All the categories listed in the table are represented except live attenuated virus, which is a traditional and widely used method that is not being tested for SARS-CoV-2. How the various categories are summarized in this table is based on the small amount of available data, combined with general experience of how similarly designed vaccines have performed against other viral pathogens. Nonetheless, there are considerable uncertainties behind some of the assessments in the table. Emerging clinical trial data will determine whether they are accurate.
- 2) Safety indicates the likelihood the vaccine will be tolerated without serious adverse effects in the absence of infection. For all categories, there are substantial uncertainties about the risk of exacerbated pathogenesis post-infection, by ADE and VAERD mechanisms (see text). These risks may be the greatest for vaccines that induce only low NAb titers, and/or a high non2054 NAb/NAb ratio.
- 3) Most emphasis has been placed on the induction of NAbs, although some data on cellular immune responses are emerging from animal studies and more will be obtained in human trials. Attempts to induce cytotoxic T-cells might include immunization with viral proteins other than S, including non-surface exposed internal ones (e.g., the N-protein). Extrapolation from other vaccines leads to the assessments listed.
- 4) N/A, not applicable. There are no known plans to produce this type of vaccine.
- 5) For a killed virus vaccine to be safe, the pathogen must be fully inactivated. Historically, inactivation has sometimes been incomplete (e.g., with polio vaccines).
- 6) Delivering DNA vaccines into muscles via electroporation is a relatively complex procedure compared to direct injection via needles or oral delivery.
- 7) The ease with which mRNA vaccines can be formulated and distributed has not been widely discussed. However, if these vaccines turn out to be unstable at ambient temperatures it will be challenging to distribute frozen or chilled stocks.
- 8) General experience suggests that producing a stable cell line and using it to make large stocks of recombinant proteins under Good Manufacturing Process conditions can take 1-2 years.

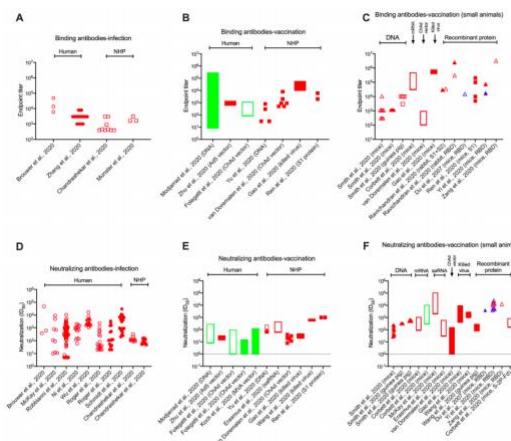


Figure 2: Magnitudes of S-protein binding antibody (ELISA) and NAb responses in COVID-19 cases and vaccinated humans and animals.

A, B, C) Anti-S protein (open symbols) and anti-RBD (closed symbols) endpoint titers; D, E, F) NAb midpoint titers (ID50) from PV assays (open symbols) and RV assays (closed symbols). In each plot, the titers for individual study subjects, or the median values for a test group, or the range recorded in a study cohort are presented. The data in panels A and D are derived from virus-infected humans and non-human primates (NHPs) and show titers obtained in the first several weeks post-symptoms. Panels B, C, E and F present data on the peak responses to S protein- or RBD-based vaccines in humans and animals. B and E, studies in humans and NHPs; C and F, studies in small animals (mice, guinea pigs, rabbits), as indicated by the labels on the x-axes. In the small-animal experiments, the immunogens used are grouped together from left to right as follows: DNA, RNA, adenovirus vectors, killed virus, recombinant S-protein or RBD protein. Data relating to SARS-CoV-2 are in red, SARS-CoV-1 in blue and MERS-CoV in green. For experimental details, the cited papers listed on the x-axes should be consulted. Assay methodologies vary between studies, which reduces the comparability of the resulting datasets. However, we judge that broad trends can still be seen. We have only included binding antibody endpoint titers and NAb midpoint (ID50) titers on the plots, excluding other methods of data representation. Multiple other papers cited in the text report on antibody responses to the S protein (or other antigens) in infected humans but do so using other formats; in those papers, the responses usually span a >1000-fold range. We note that NAb endpoint titers were presented in the following papers; the unrecorded midpoint titer values would probably be >100-fold lower: endpoint titer range <10 to ~300 for MERS-CoV DNA vaccine-immunized humans (95); median endpoint titers of 34 and 46 in RV and PV assays, respectively, for Ad5 vaccine-immunized humans (174); endpoint titer range 5-60 for SARS-CoV-2-infected rhesus macaques (97); median endpoint titer of ~40 for ChAdOx1-immunized rhesus macaques (149).

PREVENTION IN THE COMMUNITY

RISK FACTORS ASSOCIATED WITH COVID-19 INFECTION: A RETROSPECTIVE COHORT STUDY BASED ON CONTACTS TRACING

Liu T, Liang W, Zhong H, He J, Chen Z, He G, Song T, Chen S, Wang P, Li J, Lan Y, Cheng M, Huang J, Niu J, Xia L, Xiao J, Hu J, Lin L, Huang Q, Rong Z, Deng A, Zeng W, Li J, Li X, Tan X, Kang M, Guo L, Zhu Z, Gong D, Chen G, Dong M, Ma W.. Emerg Microbes Infect. 2020 Jul 1:1-31. doi: 10.1080/22221751.2020.1787799. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

Researchers at Guangdong Provincial Center for Disease Control and Prevention, China conducted a retrospective cohort study of 11,580 contacts of COVID-19 cases in the Guangdong Province from 10 January to 15 March 2020 (Figure 1) to estimate rates and risk factors for COVID-19 infection. Authors found 515 (4.4%) contacts were infected with SARS-CoV-2 (confirmed via reverse transcriptase polymerase chain reaction [RT-PCR]). Infection risks were reportedly higher in children (relative risk [RR]: 2.59, 95% CI: 1.79-3.76) and individuals aged 60-69 years (RR: 5.29, 95% CI: 3.76-7.46) compared to adults aged 20-29 years, and in females (RR: 1.66, 95% CI: 1.39-2.00) compared to males (Table 2). People having close relationship with index cases (COVID-19 suspected/confirmed) were found to be at an increased risk for infection, with an even higher risk if exposure occurred during symptomatic period (dizziness, myalgias, chills, [RR: 2.15, 95%CI: 1.67-2.79]). These findings could be useful for development of COVID-19 prevention and control measures tailored to specific at risk populations.

ABSTRACT

Objectives To estimate the attack rates, and identify the risk factors of COVID-19 infection. **Methods** Based on a retrospective cohort study, we investigated 11,580 contacts of COVID-19 cases in Guangdong Province from January 10 to March 15, 2020. All contacts were tested by RT-PCR to detect their infection of SARS-CoV-2. Attack rates by characteristics were calculated, and logistic regression was used to estimate the risk factors of infection for COVID-19. **Results** A total of 515 of 11,580 contacts were identified to be infected with SARS-CoV-2. Compared to young adults aged 20-29 years, the infected risk was higher in children (RR: 2.59, 95%CI: 1.79-3.76), and old people aged 60-69 years (RR: 5.29, 95%CI: 3.76-7.46). Females also had higher infected risk (RR: 1.66, 95%CI: 1.39-2.00). People having close relationship with index cases encountered higher risk to be infected (RR for spouse: 20.68, 95%CI: 14.28-29.95; RR for non-spouse family members: 9.55, 95%CI: 6.73-13.55; RR for close relatives: 5.90, 95%CI: 4.06-8.59; RR for other relatives: 3.37, 95%CI: 2.15-5.28). Moreover, contacts exposed to index case in symptomatic period (RR: 2.15, 95%CI: 1.67-2.79), with critically severe symptoms (RR: 1.61, 95%CI: 1.00-2.57), with symptoms of dizzy (RR: 1.58, 95%CI: 1.08-2.30), myalgia (RR: 1.49, 95%CI: 1.15-1.94), and chill (RR: 1.42, 95%CI: 1.05-1.92) had higher infected risks. **Conclusion** Children, old people, females and family members are susceptible to be infected with COVID-19, while index cases in incubation period had lower contagiousness. Our findings will be helpful for developing targeted prevention and control strategies to combat the worldwide pandemic.

FIGURES

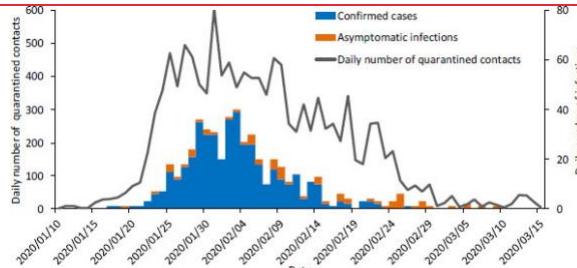


Figure 1: Daily numbers of quarantined contacts, and confirmed cases or asymptomatic infections identified from the quarantined contacts in Guangdong Province.

Characteristics	Total contacts	Total infections	Attack Rate (%)
Age of contacts (years)			
0-9	1048	60	5.7
10-19	819	33	4.0
20-29	2420	56	2.3
30-39	2601	113	4.4
40-49	1878	56	3.0
50-59	1520	76	5.0
60-69	831	92	11.1
70-79	314	21	6.7
≥80	149	7	4.7
Sex			
Male	6183	213	3.4
Female	5397	302	5.6
Relationship to the index case			
Spouse	563	131	23.3
Family members (non-spouse)	1878	199	10.6
Close relatives	1341	94	7.0
Other relatives	925	38	4.1
Social activity contacts	3344	41	1.3
Transportation contacts	2778	10	0.3
Health care workers	573	2	0.3
Others	178	0	0.0
Contacts on different transportations			
Flight	695	6	0.8
Train	901	11	1.2
Public transportation*	229	5	2.1
Private car	213	9	4.2
The Dream Cruises	63	6	9.5
Unknown	1104	14	1.3
Disease history of confirmed index cases#			
Incubation period	2211	72	3.3
Symptomatic period	5904	411	7.0
Contacts to the index cases at different time (days to the symptom onset)*			
≤-5	522	9	1.7
-4 to -3	283	6	2.1
-2 to -1	974	25	2.5
0	1020	61	5.6
1 to 2	1036	81	7.3
3 to 4	865	97	10.1
5 to 6	702	61	8.0
7 to 8	371	31	7.7
9 to 10	223	16	6.7
11 to 12	106	6	5.4
13 to 14	109	4	3.5
15 to 16	188	10	5.1
≥17	265	11	4.0
Clinical severity of index case			
Mild	1244	57	4.6
Moderate	5637	344	6.1
Severe	812	52	6.4
Critically severe	371	28	7.5

Table 2: Attack rates of COVID-19 in contacts with different characteristics.

SOCIAL DISTANCING AS A HEALTH BEHAVIOR: COUNTY-LEVEL MOVEMENT IN THE UNITED STATES DURING THE COVID-19 PANDEMIC IS ASSOCIATED WITH CONVENTIONAL HEALTH BEHAVIORS

Bourassa KJ, Sbarra DA, Caspi A, Moffitt TE.. Ann Behav Med. 2020 Jul 1:kaaa049. doi: 10.1093/abm/kaaa049. Online ahead of print.

Level of Evidence: Other - Modeling

BLUF

This study examined personal and health behavior factors (detailed in summary below) and evaluated their correlation with reduction in movement outside the home during the COVID-19 pandemic across 2,858 US counties (Figure 1), finding that

counties with individuals who have better health behaviors, more wealth, education, and advanced age have a more positive correlation with staying close to home during the pandemic (Table 2). The authors believe these results indicate that existing health behavior literature can be applied to public health education efforts during the COVID-19 pandemic to reduce transmission.

SUMMARY

This study, using data collected from Cuebiq and Streetlight Data from March 1, 2020 to April 7, 2020, examined the correlation between preexisting health behaviors (i.e. physical activity, smoking, obesity, flu vaccination, and mammography screening rates) and reduction in movement outside the home during the COVID-19 pandemic across 2,858 US counties (Figure 1) via mixed effect linear models. Findings revealed that counties with healthier behaviors had a more positive correlation with reduction in movement, measured as daily vehicle miles traveled and percentage of people staying within 1 mile of their home, than in counties with less healthy behavior patterns. The authors also used mixed linear models to examine county and state level models using control variables such as race/ethnicity, age, gender, household income, education, population, and presence of stay-at-home orders. In terms of counties, those with more limited movement were seen to be more educated, wealthier, urban, and with an older population (Table 2). While the authors recommend more studies to better understand individual-led behavior, they do recognize that conventional health behaviors are a good determinant of social distancing behavior.

ABSTRACT

BACKGROUND: Social distancing-when people limit close contact with others outside their household-is a primary intervention available to combat the COVID-19 pandemic. The importance of social distancing is unlikely to change until effective treatments or vaccines become widely available. However, relatively little is known about how best to promote social distancing. Applying knowledge from social and behavioral research on conventional health behaviors (e.g., smoking, physical activity) to support public health efforts and research on social distancing is promising, but empirical evidence supporting this approach is needed. **PURPOSE:** We examined whether one type of social distancing behavior-reduced movement outside the home-was associated with conventional health behaviors. **METHOD:** We examined the association between GPS-derived movement behavior in 2,858 counties in USA from March 1 to April 7, 2020 and the prevalence of county-level indicators influenced by residents' conventional health behaviors. **RESULTS:** Changes in movement were associated with conventional health behaviors, and the magnitude of these associations were similar to the associations among the conventional health behaviors. Counties with healthier behaviors-particularly less obesity and greater physical activity-evidenced greater reduction in movement outside the home during the initial phases of the pandemic in the USA. **CONCLUSIONS:** Social distancing, in the form of reduced movement outside the home, is associated with conventional health behaviors. Existing scientific literature on health behavior and health behavior change can be more confidently used to promote social distancing behaviors during the COVID-19 pandemic.

FIGURES

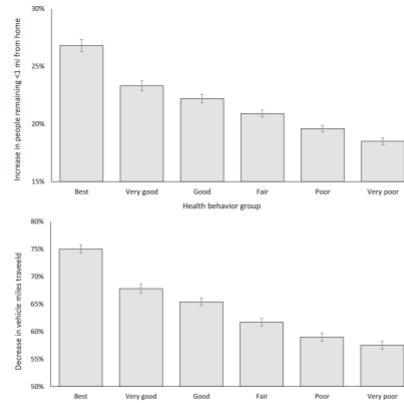


Fig. 1. Change in movement behavior from the first week of March to the first week of April. Counties were categorized by the health behavior composite, which was z-scored. *Best* were 1.0 SD or more above the mean ($n = 473$, 16.6%), *Very good* = between 0.5 and 1 SD ($n = 308$, 13.9%), *Good* = between the mean and 0.5 SD ($n = 532$, 18.6%), *Fair* = the mean ($n = 544$, 19.0%), *Poor* = between -0.5 and -1 SD below the mean ($n = 486$, 17.0%), *Very poor* <-1 SD below the mean ($n = 425$, 14.9%). Error bars represent 95% confidence intervals.

Table 2. Mixed effect model results predicting change in movement behaviors

N = 2,858	Increase in % of people remaining <1 mile from home		Decrease in vehicle miles traveled	
	β	95% CI	β	95% CI
County-level predictors				
Health behavior composite	0.11*	[0.02, 0.21]	0.16**	[0.09, 0.24]
March baseline	-0.32**	[-0.38, -0.26]	0.05	[-0.02, 0.12]
Population size	0.10*	[0.02, 0.19]	-0.01	[-0.07, 0.05]
Rurality	-0.10**	[-0.16, -0.06]	-0.28**	[-0.33, -0.24]
Household income	0.46**	[0.39, 0.54]	0.16**	[0.11, 0.22]
Education	0.23**	[0.18, 0.27]	0.37**	[0.31, 0.43]
Age	0.08**	[0.03, 0.14]	0.07*	[0.02, 0.13]
Ethnicity	-0.17**	[-0.27, -0.07]	-0.08*	[-0.15, -0.01]
Gender	0.01	[-0.02, 0.03]	-0.00	[-0.04, 0.04]
State-level predictors				
Stay-at-home order issued	0.50**	[0.31, 0.69]	0.30*	[0.06, 0.54]
Population size	-0.01	[-0.18, 0.17]	-0.00	[0.22, 0.21]
Rurality	0.11	[-0.21, 0.44]	0.18	[-0.21, 0.57]

Models nested counties within states. "March baseline" represents the average of the outcomes over the first week of March. Rurality is coded as percent of the county or state that is rural. Ethnicity is coded as percentage non-Hispanic whites. Education is coded as percent with some college education. Gender is coded as percentage women. "Stay-at-home order issued" assessed whether the state issued a stay-at-home order.

* $p \leq .05$.

** $p \leq .01$.

PREVENTION IN THE HOSPITAL

SARS-COV-2 ENVIRONMENTAL CONTAMINATION ASSOCIATED WITH PERSISTENTLY INFECTED COVID-19 PATIENTS

Lei H, Ye F, Liu X, Huang Z, Ling S, Jiang Z, Cheng J, Huang X, Wu Q, Wu S, Xie Y, Xiao C, Ye D, Yang Z, Li Y, Leung NHL, Cowling BJ, He J, Wong SS, Zanin M.. Influenza Other Respir Viruses. 2020 Jun 24. doi: 10.1111/irv.12783. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

A study conducted in Guangzhou, China in April of 2020 tested for hospital environmental contamination of SARS-CoV-2 in 218 ICUs and 182 isolation wards using RT-PCR of air and surface samples. They found that ICUs had much lower presence of viral RNA, presumably due to more stringent infection control measures, and isolation wards had much higher levels of viral RNA. Since the study's methods could not differentiate between viable viral particles, the authors recommend healthcare workers to remain hypervigilant during the pandemic.

ABSTRACT

BACKGROUND: Severe COVID-19 patients typically test positive for SARS-CoV-2 RNA for extended periods of time, even after recovery from severe disease. Due to the timeframe involved, these patients may have developed humoral immunity to SARS-CoV-2 whilst still testing positive for viral RNA in swabs. Data is lacking on exposure risks in these situations. Here we studied SARS-CoV-2 environmental contamination in an ICU and an isolation ward caring for such COVID-19 patients. **METHODS:** We collected air and surface samples in a hospital caring for critical and severe COVID-19 cases from common areas and areas proximal to patients. **RESULTS:** Of the 218 ICU samples, an air sample contained SARS-CoV-2 RNA. Of the 182 isolation ward samples, nine contained SARS-CoV-2 RNA. These were collected from a facemask, the floor, mobile phones and the air in the patient room and bathroom. Serum antibodies against SARS-CoV-2 were detected in these patients at the beginning of the study. **CONCLUSIONS:** Whilst there is a perception of increased risk in the ICU, our study demonstrates that isolation wards may pose greater risks to healthcare workers and exposure risks remain with clinically-improved patients, weeks after their initial diagnoses. As these patients had serum antibodies, further studies may be warranted to study the utility of serum antibodies as a surrogate of viral clearance in allowing people to return to work. We recommend continued vigilance even with patients who appear to have recovered from COVID-19.

DECONTAMINATION METHODS FOR REUSE OF FILTERING FACEPIECE RESPIRATORS

Su-Velez BM, Maxim T, Long JL, St John MA, Holliday MA.. JAMA Otolaryngol Head Neck Surg. 2020 Jul 2. doi: 10.1001/jamaoto.2020.1423. Online ahead of print.

Level of Evidence: 4 - Review / Literature Review

BLUF

A literature review by physicians affiliated with David Geffen School of Medicine at UCLA and Greater Los Angeles Veterans Administration Healthcare System found that UV light, steam heating, dry heat, and commercial sterilization methods with ethylene oxide or vaporized hydrogen peroxide were optimal decontamination methods for preserving and reusing N95

respirators (Table 1). The authors also provide recommended protocols for donning/doffing (Box 1) and preservation/reuse of N95 respirators (Box 2), urging health professionals, especially otolaryngologists, to utilize effective decontamination methods when reusing PPE.

ABSTRACT

Importance: The novel coronavirus disease 2019 (COVID-19) has proven to be highly infectious, putting health care professionals around the world at increased risk. Furthermore, there are widespread shortages of necessary personal protective equipment (PPE) for these individuals. Filtering facepiece respirators, such as the N95 respirator, intended for single use, can be reused in times of need. We explore the evidence for decontamination or sterilization of N95 respirators for health care systems seeking to conserve PPE while maintaining the health of their workforce. **Observations:** The filtration properties and fit of N95 respirators must be preserved to function adequately over multiple uses. Studies have shown that chemical sterilization using soap and water, alcohols, and bleach render the respirator nonfunctional. Decontamination with microwave heat and high dry heat also result in degradation of respirator material. UV light, steam, low-dry heat, and commercial sterilization methods with ethylene oxide or vaporized hydrogen peroxide appear to be viable options for successful decontamination. Furthermore, since the surface viability of the novel coronavirus is presumed to be 72 hours, rotating N95 respirator use and allowing time decontamination of the respirators is also a reasonable option. We describe a protocol and best practice recommendations for redoffing decontaminated N95 and rotating N95 respirator use. **Conclusions and Relevance:** COVID-19 presents a high risk for health care professionals, particularly otolaryngologists, owing to the nature of viral transmission, including possible airborne transmission and high viral load in the upper respiratory tract. Proper PPE is effective when used correctly, but in times of scarce resources, institutions may turn to alternative methods of preserving and reusing filtering facepiece respirators. Based on studies conducted on the decontamination of N95 respirators after prior outbreaks, there are several options for institutions to consider for both immediate and large-scale implementation.

FIGURES

Box 1. Recommended Protocol for Donning and Doffing N95 Respirators Treated for Decontamination
<ol style="list-style-type: none">1. Perform hand hygiene before donning N95 respirator<ul style="list-style-type: none">• Use soap and water or alcohol-based hand sanitizer2. Inspect the N95 for any evidence of physical damage<ul style="list-style-type: none">• Look for broken straps, tears in the material, loosened nosepiece, etc.3. Don N95 respirator and check fit<ul style="list-style-type: none">• Refer to institution's or respirator manufacturer's guidelines for fit testing and specific instructions• N95 respirator should always be worn with eye protection4. Keep the N95 respirator clean; use additional barriers to prevent soiling<ul style="list-style-type: none">• Use surgical mask or face-shield over the N95 respirator to prevent soiling• Always wear eye protection• Wear N95 respirator as long as possible; avoid doffing5. Perform hand hygiene before doffing<ul style="list-style-type: none">• Use soap and water or alcohol-based hand sanitizer6. Doff mask into a clean paper bag clearly marked with the date<ul style="list-style-type: none">• Preload paper bag into a plastic bag for ease of transport to health care professional's designated storage space• Perform hand hygiene for prevention of any moisture• Avoid touching outside of mask; use straps when handling7. Perform hand hygiene<ul style="list-style-type: none">• N95 respirator is used and may be contaminated8. Store bag in designated storage space<ul style="list-style-type: none">• Use a locker, container in vehicle trunk, etc.• Do not store other materials in this storage space that may directly contact paper bags9. To prevent cross-contamination, only 1 N95 respirator should be stored in each bag10. Perform hand hygiene after donning used respirator11. Avoid touching or adjusting N95 respirator throughout session of use<ul style="list-style-type: none">• Hand hygiene should be performed any time the N95 respirator is touched or adjusted• Immediately discard any respirator that becomes grossly contaminated with blood, respiratory secretions, or other bodily fluids from patients• The maximum recommended number of days of N95 respirator reuse is 512. Perform hand hygiene after removing gloves13. Check respirator seal before removing gloves14. Perform hand hygiene after removing used respirator15. Avoid touching or adjusting N95 respirator throughout session of use<ul style="list-style-type: none">• Hand hygiene should be performed any time the N95 respirator is touched or adjusted• Immediately discard any respirator that becomes grossly contaminated with blood, respiratory secretions, or other bodily fluids from patients• The maximum recommended number of days of N95 respirator reuse is 5

Box 2. Recommended Protocol for Preservation and Reuse of N95 Respirators
<ol style="list-style-type: none">1. Perform hand hygiene before donning N95 respirator<ul style="list-style-type: none">• Use soap and water or alcohol-based hand sanitizer2. Inspect the N95 respirator or any evidence of physical damage<ul style="list-style-type: none">• Look for broken straps, tears in the material, loosened nosepiece, etc.3. Don N95 respirator and check fit<ul style="list-style-type: none">• Refer to the institution's or respirator manufacturer's guidelines for fit testing and specific instructions• N95 respirator should always be worn with eye protection4. Keep the N95 respirator clean; use additional barriers to prevent soiling<ul style="list-style-type: none">• Use surgical mask or face-shield over the N95 respirator to prevent soiling• Always wear eye protection• Wear N95 respirator as long as possible; avoid doffing5. Perform hand hygiene before doffing<ul style="list-style-type: none">• Use soap and water or alcohol-based hand sanitizer6. Doff mask into a clean paper bag clearly marked with the date<ul style="list-style-type: none">• Preload paper bag into a plastic bag for ease of transport to health care professional's designated storage space• Perform hand hygiene for prevention of any moisture• Avoid touching outside of mask; use straps when handling7. Perform hand hygiene<ul style="list-style-type: none">• N95 respirator is used and may be contaminated8. Store bag in designated storage space<ul style="list-style-type: none">• Use a locker, container in vehicle trunk, etc.• Do not store other materials in this storage space that may directly contact paper bags9. Label with name if necessary to avoid cross-contamination10. Store bag with N95 respirator for at least 3 d (72 h) or up to 7 d<ul style="list-style-type: none">• After this amount of time, the severe acute respiratory syndrome coronavirus 2 virus has reduced infectivity after at least 72 h on porous surfaces11. Before doffing a used N95 respirator, inspect the respirator carefully again to ensure no damage<ul style="list-style-type: none">• Wear gloves (nonsterile) to don a used N95 respirator.• Avoid touching the inside of the respirator• Discard any respirator that is obviously damaged or hard to breathe through• Check respirator seal before removing gloves12. Perform hand hygiene after donning used respirator<ul style="list-style-type: none">• Used respirator is assumed to potentially still harbor some infectious material• Avoid touching or adjusting N95 respirator throughout session of use• Hand hygiene should be performed any time the N95 respirator is touched or adjusted• Immediately discard any respirator that becomes grossly contaminated with blood, respiratory secretions, or other bodily fluids from patients• The maximum recommended number of days of N95 respirator reuse is 513. Stockpile of used N95 respirators can be rotated approximately every 72 h or longer (ie, 3 per 72-hour cycle)

Table 1. Summary of Decontamination Methods for N95 Respirators

Technique	Protocol	Duration	Advantages	Disadvantages	Effect on filtration	Evidence
Time decontamination	Doff used N95 respirator, remove clean paper bag, store in designated space until reuse	At least 72 h, feasible if dry possible (5–7 d ideal)	Simple, low-cost, easiest to implement	Unproven, requires time for reuse, requires adequate supply for rotation	Minimal, secondary to reuse	Not reviewed ^a but based on studies by van Doremalen et al. ²⁹ 2020; Kampf et al. ³⁴ 2020; Lai et al. ³⁵ 2020; Otter et al. ³⁶ 2015; endorsed by CDC ³⁹
Chemical decontamination						
Bleach ^b	Submerge N95 respirator mask in 0.5% bleach solution, rinsing with water, dry overnight	Treat 30 min then dry 16-h	Toxic to coronaviruses, readily available, low cost	Residual toxic, unpleasant odor	Aerosol penetration met NIOSH certification criteria	Peer-reviewed: Viscusi et al. ²³ 2009; Kampf et al. ³⁴ 2020
Alcohols ^b	Submerge N95 respirator in solution of 70%–95% alcohol, dry	Soak 20 min, then dry 72 h	Toxic to coronaviruses, readily available, low cost	Rendered respirator filter ineffective	Filtration efficiency significantly degraded	Peer-reviewed: Viscusi et al. ²³ 2007; Kampf et al. ³⁴ 2020
Soap and water ^b	Soak N95 respirator in Ivory bar soap, 1:9 dilution with water and diluted in tap water, dry	Soak 20 min, then dry 72 h	Readily available, low cost	Rendered respirator filter ineffective	Filtration efficiency significantly degraded	Peer-reviewed: Viscusi et al. ²³ 2007
Vaporized hydrogen peroxide	STERI-MAD 100% H ₂ O ₂ gas plasma sterilizer, single 55-min standard cycle	55 min	Commercially available, fast turnaround	Cellulose-based product (ie, cotton in certain brands) may interfere with sterilization	Aerosol penetration met NIOSH certification criteria	Peer-reviewed: Viscusi et al. ²³ 2009; Not peer-reviewed: Fisher et al. ⁴⁰ 2020; Fischer et al. ⁴² 2020
Ethylene oxide ^b	Steri-Vac 5XL: single warm cycle (55 °C) and 100% ethylene oxide gas, followed by aeration	Ethylene oxide 1 h, then 4-h aeration	Commercially available	Lengthy protocol may limit overall capacity; residual chemicals present	Aerosol penetration met NIOSH certification criteria	Peer-reviewed: Viscusi et al. ²³ 2009; Salter et al. ⁴³ 2010
Heat decontamination						
Microwave steam	1100–1250 W-Microwave; individual N95 respirator placed on top of a shallow 50 mL water, or commercially available steam bag (Medela) with 60 mL water	Microwave 3.5–2 min at full power, then drying time (60 min)	Fast turnaround, materials commercially available	Requires individual mask sterilization, may be difficult to scale up	Filtration efficiency remains 95%	Peer-reviewed: Fisher et al. ⁴¹ 2011; Lore et al. ²⁰ 2012
Microwave oven heat	1100W microwave at full power; individual N95 respirator placed on a paper towel over revolving glass plate	2 min total [1 min per side of mask]	Commercially available, fast turnaround	Mask material melted after treatment	Unable to test filtration owing to melted components	Peer-reviewed: Viscusi et al. ²³ 2009
Dry oven heat	Heat N95 respirator for 30 min at 70–150 °C in oven	30-min treatment	>99% effective against Escherichia coli, relatively fast	Temperatures >100 °C may cause mask to melt	Filtration efficiency remains 95% at 70°C, degraded at 150°C	Peer-reviewed: Viscusi et al. ²³ 2009; Non-peer-reviewed: Price and Chu ⁴² 2020; Fischer et al. ⁴² 2020
Hot water vapor/moist heat	Treat N95 respirator with hot water vapor from laundry machine or moist heat at 65 °C	10–20 min treatment	>99% effective against E. coli, fast treatment, low cost	Protocol not well described, not proven against viruses	Filtration efficiency remains high	Peer-reviewed: Lore et al. ²⁰ 2012; Non-peer-reviewed: Price and Chu ⁴² 2020
UV light decontamination						
UVGI	Protocols vary; UV light applied to 1 or both sides of N95 respirator; UVGI studied at exposures ranging from 2 to 950 J/cm ²	1–10-min exposure	Multiple studies suggesting dose-dependent, protocol for clinical use already pioneered	Variability in protocols, dose, concentration, dose, parts of mask (straps) may take longer to decontaminate, high dose UV may degrade mask	Aerosol penetration met NIOSH certification criteria	Peer-reviewed: Li et al. ⁴⁴ 2016; Liu et al. ⁴⁵ 2015; Viscusi et al. ²³ 2009; Non-peer-reviewed: Li et al. ⁴⁶ 2020; Fischer et al. ⁴² 2020; Fischer et al. ⁴² 2020

Abbreviations: NIOSH, National Institute for Occupational Safety and Health; UVGI, UV germicidal irradiation.

^a The studies are peer reviewed on likely survival time of virus on surfaces; however, the technique of using time as a decontamination method has not been tested or validated.

^b These decontamination methods are not recommended for consideration owing to the risk of toxic residual chemicals or degradation in respirator function.

PROTECTION OF HEALTHCARE WORKERS AGAINST COVID-19 AT A LARGE TEACHING HOSPITAL IN SEOUL, KOREA

Jeon YW, Park ES, Jung SJ, Kim Y, Choi JY, Kim HC.. Yonsei Med J. 2020 Jul;61(7):631-634. doi: 10.3349/ymj.2020.61.7.631. Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

Authors from Seoul, South Korea report that there was no COVID-19 transmission to Severance Hospital employees after 184 hospital employees came into contact with 13 asymptomatic COVID-19 patients between February 29 and March 27, 2020 (Table 2). Employees at risk were classified into four risk levels and assigned to a specific management plan (Table 1). The authors suggest that the preventative strategies taken at this hospital were effective and urge other hospitals to also establish similar efficient strategies to protect healthcare workers (Table 1).

ABSTRACT

Thirteen patients with coronavirus disease 2019 (COVID-19) visited a university hospital in Seoul before recognizing their disease infections, causing contact with 184 hospital workers. We classified the patients into four risk levels and provided corresponding management measures. At 31 days after the last event, all screening laboratory results were negative, and no symptoms/signs were reported.

FIGURES

YMJ

Protection of Hospital Workers Against COVID-19

Table 1. Risk Classification and Management Plan for Healthcare Workers in Possible Contact with COVID-19 Patients

Risk level	Management plan	Possible contact	Protection of healthcare workers
3	Self-quarantine*	Close contact with a COVID-19 patient not wearing face mask Aerosol-generating procedures [†] Direct physical contact [‡]	Without four-item-set of PPE ^{††} Without four-item-set of PPE ^{††} Without four-item-set of PPE ^{††}
2	Active monitoring [§]	Contact within 2 meters in closed space Contact within 2 meters in open space	Not wearing respirator [¶]
1	Passive monitoring [§]	Minimal contact**	Not wearing respirator
0	Usual management [§]	Any types of contact No possibility of close contact ^{**}	With four-item-set of PPE ^{††} Not applicable

COVID-19, coronavirus disease 2019; PPE, personal protective equipment; RT-PCR, reverse transcription-polymerase chain reaction.

*Daily monitor of COVID-19 patient, including RT-PCR virus tests on day 1 and day 14, self-quarantine for 14 days, “Daily checklist of COVID-19 related symptoms/signs: RT-PCR virus tests on day 1 and day 14, self-quarantine for 14 days, COVID-19 related symptoms/signs: RT-PCR virus test, Routine screening at the same level as other hospital staff; RT-PCR virus tests upon request, including open suctioning of respiratory tract, intubation, bronchoscopy, and cardio-pulmonary resuscitation.” **including vital sign check-up, blood sampling, potential contact with patient’s body fluid, and therapies requiring physical contact, *Brief or distant (<2 m) contact with a COVID-19 patient while wearing face masks. “No possibility of close contact, but working in the same department when a COVID-19 patient visits. §Personal protective equipment consisting of gloves, long-sleeved gowns, eye protection, and fit-tested respirator. **N95/K94 certified by Korea Food & Drug Administration, which filters at least 95% of 0.4 µm-sized particle or equivalent. ¶Surgical/dental mask or equivalent.

Table 2. Classification of Healthcare Workers who Came in Contact with COVID-19 Patients

Variables	Total (n=194)	Risk level			
		Level 0 (n=145)	Level 1 (n=17)	Level 2 (n=9)	Level 3 (n=13)
Age (yr), median [min-max]	29 [21-66]	29 [22-66]	37 [21-58]	29 [23-41]	27 [24-56]
Sex					
Male	58 (31.5)	43 (29.7)	7 (41.2)	4 (44.4)	4 (30.8)
Female	126 (68.5)	102 (70.3)	10 (56.8)	5 (55.6)	9 (69.2)
Occupation					
Physicians	32 (17.4)	27 (18.6)	2 (11.8)	-	3 (23.1)
Nurses	60 (32.6)	50 (34.5)	4 (23.5)	-	6 (46.2)
Therapists	45 (24.5)	40 (27.6)	-	5 (55.6)	-
Radiologic technologists	11 (6.0)	9 (6.2)	2 (11.8)	-	-
Hospital porters	11 (6.0)	9 (6.2)	1 (5.9)	-	1 (7.7)
Hospital administrators	5 (2.7)	2 (1.4)	3 (17.6)	-	-
Maintenance workers	3 (1.6)	2 (1.4)	-	-	1 (7.7)
Security guards	13 (7.1)	5 (3.4)	3 (17.6)	3 (33.3)	2 (15.4)
Others*	4 (2.2)	1 (0.7)	2 (11.8)	1 (11.1)	-
Face mask/respirator					
N95/KF94†	92 (50.0)	80 (55.2)	2 (11.8)	4 (44.4)	6 (46.2)
Dental	61 (33.2)	35 (24.1)	15 (88.2)	5 (55.6)	6 (46.2)
Not equipped	2 (1.1)	1 (0.7)	-	-	1 (7.7)
Undetermined	29 (15.8)	29 (20.0)	-	-	-
Site of exposure					
Emergency room	80 (43.5)	69 (47.6)	-	4 (44.4)	7 (53.8)
Inpatient wards	6 (3.2)	-	-	-	6 (46.2)
Outpatient clinics	21 (11.4)	16 (11)	5 (29.4)	-	-
COVID-19 screening center	19 (10.3)	17 (11.7)	2 (11.8)	-	-
Rehabilitation center	45 (24.5)	40 (27.6)	-	5 (55.6)	-
Others	13 (7.1)	3 (2.1)	10 (58.8)	-	-
Number of RT-PCR test‡					
Twice	47 (25.5)	26 (17.9)§	-	9 (100.0)	12 (92.3)
Once	79 (42.9)	62 (42.8)§	16 (94.1)	-	1 (7.7)
None	58 (31.5)	57 (39.3)	1 (5.9)	-	-

COVID-19, coronavirus disease 2019; RT-PCR, reverse transcription-polymerase chain reaction.

Values are number (%), if not indicated otherwise.

*Including medical technicians in the emergency room, ambulance drivers, in-hospital pharmacists, and convenience store cashiers. †KF94 is a respirator certified by Korea Food & Drug Administration, which filters at least 94% of 0.4 µm-sized particles. ‡RT-PCR virus tests for SARS-CoV-2 on nasopharyngeal swab; all results were negative. §RT-PCR virus tests were performed upon request for a part of the group.

MANAGEMENT

DISCHARGED COVID-19 PATIENTS TESTING POSITIVE AGAIN FOR SARS-COV-2 RNA: A MINIREVIEW OF PUBLISHED STUDIES FROM CHINA

Han Z, Battaglia F, Terlecky SR.. J Med Virol. 2020 Jul 1. doi: 10.1002/jmv.26250. Online ahead of print.

Level of Evidence: 4 - Review / Literature Review

BLUF

A review of 12 reports involving a total of 90 patients in China who re-tested positive for SARS-CoV-2 via RT-PCR testing after discharge found that these patients were largely asymptomatic and re-tested positive despite proper discharge protocol (i.e. 2 negative results for SARS-CoV-2 RT-PCR 24 hours apart). Although the reasons for this phenomenon remain uncertain, the authors suggest testing respiratory and fecal samples simultaneously when discharging COVID-19 patients and educating patients on post-discharge quarantine, social distancing, and appropriate follow-up protocol.

ABSTRACT

In the ongoing COVID-19 pandemic, one potential cause of concern is that some discharged COVID-19 patients are testing positive again for SARS-CoV-2 RNA. To better understand what is happening and to provide public health policy planners and clinicians timely information, we have searched and reviewed published studies about discharged patients testing positive again for the SARS-CoV-2 RNA. Our search found 12 reports, all of which described patients in China. Our review of these reports indicates the presence of discharged patients who remain asymptomatic but test positive. However, it is unclear whether they are contagious because a positive RT-PCR test does not necessarily indicate the presence of replicating and transmissible virus. Our review suggests the need for timely, parallel testing of different samples, including for example, fecal specimens, from COVID-19 patients before and after they are discharged from hospitals. This article is protected by copyright. All rights reserved.

ACUTE CARE

RETROSPECTIVE STUDY OF RISK FACTORS FOR MYOCARDIAL DAMAGE IN PATIENTS WITH CRITICAL CORONAVIRUS DISEASE 2019, IN WUHAN

Li L, Zhang S, He B, Chen X, Zhao Q.. J Am Heart Assoc. 2020 Jun 30:e016706. doi: 10.1161/JAHA.120.016706. Online ahead of print.

Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

A retrospective cohort study from February 1 to February 24, 2020 conducted at Renmin University Hospital in China found that patients with COVID-19-related myocardial damage (n=34) had associated risk factors of old age (greater than 70 years), high C-reactive protein (greater than 100 mg/L), increased lactate dehydrogenase U/L (greater than 300U/L), and high plasma lactic acid (greater than 3 mmol/L) as compared to those without myocardial injury (n=48; Table 5). Although limited by a small sample size, this study suggests that physicians should be aware of myocardial damage and associated risk factors among patients with critical COVID-19.

ABSTRACT

Background The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) threatens human health and the mortality rate is higher in patients who develop myocardial damage. However, the possible risk factors for myocardial damage in patients with coronavirus disease 2019 (COVID-19) are not fully known. **Methods and Results** Critical type patients were selected randomly from 204 confirmed COVID-19 cases occurring in Renmin Hospital of Wuhan University, from February 1, 2020 to February 24, 2020. Univariate analyses were used to compare the two groups: the myocardial damage group and the non-myocardial damage group. A total of 82 critical patients with COVID-19 were recruited: 34 with myocardial damage and 48 without myocardial damage. Thirty patients died in the myocardial damage group, and 20 died in the non-myocardial damage group. In univariate analysis, the proportion of elderly patients (>70 y: 70.59% vs 37.50%; P=0.003) and patients with cardiovascular disease (41.18% vs 12.50%; P=0.003) was higher among myocardial damage patients than among non-myocardial damage patients. Multivariate analysis showed that age>70 years old (HR 2.44, 95% CI 1.01-5.40), C-reactive protein greater than 100 mg/L (HR 1.92, 95% CI 0.94-3.92), lactate dehydrogenase greater than 300 U/L (HR 2.67, 95% CI

1.03-6.90), and lactic acid greater than 3 mmol/L (HR 3.25, 95% CI 1.57-6.75) were independent risk factors for myocardial damage in patients with COVID-19. Conclusions Old age (>70 years), C-reactive protein greater than 100 mg/L, lactate dehydrogenase greater than 300 U/L and lactic acid greater than 3 mmol/L are high-risk factors related to myocardial damage in critical patients with COVID-19.

FIGURES

Characteristics	coefficient	Standard error (coefficient)	wald	P-value	HR(95%CI)
Age>70yrs	0.891	0.406	4.810	0.028	2.44(1.01-5.40)
Lactate hydrogenase>300U/L	0.981	0.485	4.091	0.043	2.67(1.03-6.90)
C-reactive protein>100mg/L	0.650	0.365	3.165	0.075	1.92(0.94-3.92)
Lactic acid>3mmol/L	1.179	0.373	10.022	0.002	3.25(1.57-6.75)

HR: hazard ratio

CI: confidence interval

Table 5. Cox proportional hazards regression model of risk factors for myocardial damage with COVID-19.

ACUTE MYOPERICARDITIS WITH PERICARDIAL EFFUSION AND CARDIAC TAMPONADE IN A PATIENT WITH COVID-19

Purohit R, Kanwal A, Pandit A, Patel BM, Meininger GR, Brown JJ, Kaliyadan AG, Saini A.. Am J Case Rep. 2020 Jul 1;21:e925554. doi: 10.12659/AJCR.925554.

Level of Evidence: 5 - Case report

BLUF

An 82-year-old woman who received care in Baltimore, Maryland, USA with a history of paroxysmal atrial fibrillation, hypertension, hyperlipidemia, and iron-deficiency anemia developed myocarditis and tamponade in the setting of RT-PCR confirmed COVID-19. An initial echocardiogram revealed a small pericardial effusion, but seven days later, after the patient reported chest tightness and dyspnea, a repeat echo showed an enlarged effusion and tamponade requiring pericardiocentesis (Figure 3). The patient has since improved clinically without needing mechanical ventilation during hospitalization. The authors posit that physicians need to be prepared for this complication even in patients without the typical pulmonary manifestations of COVID-19.

ABSTRACT

BACKGROUND Coronavirus disease 2019 (COVID-19) is primarily a respiratory illness. However, with rising numbers of cases, multiple reports of cardiovascular manifestations have emerged. We present a case of COVID-19 infection complicated by myopericarditis and tamponade requiring drainage. **CASE REPORT** An 82-year-old woman with multiple comorbidities presented with five days of productive cough, fever with chills, and intermittent diarrhea. She tested positive for COVID-19. Index EKG revealed new diffuse T-wave inversions and a prolonged QT interval (>500 ms). Troponin was mildly elevated without any anginal symptoms. Hydroxychloroquine and azithromycin were not initiated due to concerns about QT prolongation. The echocardiogram revealed preserved left ventricular (LV) function, a small global pericardial effusion, and apical hypokinesis. Serial echocardiograms revealed an enlarging circumferential pericardial effusion with pacemaker wire reported as 'piercing' the right ventricular (RV) apex alongside early diastolic collapse of the right ventricle, suggesting echocardiographic tamponade. Chest CT revealed extension of the RV pacemaker lead into the pericardial fat. Interestingly, on comparison with a previous chest CT from 2019, similar lead positions were confirmed. Pericardiocentesis was performed with removal of 400 cc exudate. **CONCLUSIONS** Acute myopericarditis and pericardial effusion can occur in COVID-19 infection, even in the absence of severe pulmonary disease. This case highlights the importance of awareness of rare cardiac manifestations of COVID-19 in the form of acute myopericarditis and cardiac tamponade and their early diagnosis and management.

FIGURES

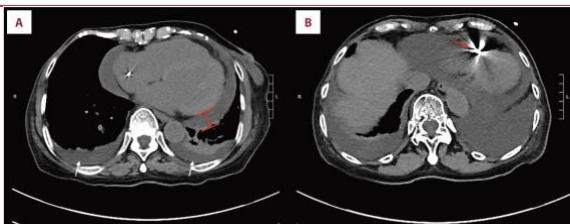


Figure 3. Chest CT showing significant circumferential pericardial effusion and bilateral pleural effusions (A) with right ventricular pacemaker lead tip possibly in pericardial space (red arrow - B).

CRITICAL CARE

EARLY DATA FROM CASE SERIES OF TRACHEOSTOMY IN PATIENTS WITH SARS-COV-2

Floyd E, Harris SS, Lim JW, Edelstein DR, Filangeri B, Bruni M.. Otolaryngol Head Neck Surg. 2020 Jun 30:194599820940655. doi: 10.1177/0194599820940655. Online ahead of print.

Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

This retrospective cohort study conducted at North Shore University Hospital and Lenox Hill Hospital between April 1-30, 2020 describes the clinical outcome of 38 COVID-19 patients who underwent tracheostomies as well as SARS-CoV-2 serostatus of the healthcare workers performing the procedures. They found that as of May 14, 2020 55% of patients (n=21) had weaned from ventilators, 18.4% had undergone decannulation (n=7), and 5.3% expired for reasons unrelated to surgery (n=2)(Table 1); no surgeons seroconverted. The authors elaborate on PPE (see summary) and believe tracheostomy is a useful intervention but recommend larger studies for definitive recommendations.

SUMMARY

The authors believe tracheostomy can facilitate ventilator weaning and shorten ICU stays and considered this intervention for patients after at least 14 days of intubation based on clinical judgment, without specific inclusion/exclusion criteria (see Table 1 for results). Tracheostomies cause aerosolization and the authors detailed specific PPE protocols; staff involved in the procedure wore face shields, N95 masks covered with surgical masks, gowns, and coverings for hair and shoes in negative pressure or HEPA filtered rooms when possible. All attending surgeons performing tracheostomies on patients admitted for COVID-19 (n=10) underwent SARS-CoV-2 antibody testing 6 weeks after the initial tracheostomies and 2 weeks after the last tracheostomies included in this analysis; none seroconverted. The authors believe this supports the safety of this intervention but additional studies are needed.

ABSTRACT

Thirty-eight tracheostomies were performed on patients with respiratory failure secondary to SARS-CoV-2 infection over the month of April at North Shore University Hospital and Lenox Hill Hospital (members of Northwell Health System in Long Island and New York City). Follow-up by May 14 revealed that 21 (55.2%) had been weaned from ventilators and 7 (18.4%) underwent decannulation. Two patients (5.3%) expired in the weeks following tracheostomy. Between the 2 institutions, 10 attending surgeons performed all of the tracheostomies using appropriate personal protective equipment, and none demonstrated seroconversion within 1 to 2 weeks of this article.

FIGURES

Table 1. Patients Weaned to Tracheostomy Collar vs Those Who Remained Ventilator Dependent at Lenox Hill Hospital and North Shore University Hospital.^a

	Weaned (n = 21)	Ventilator dependent (n = 17)
Age, y	62 (56-73)	69 (62-79)
Sex		
Male	14 (66.7)	10 (58.8)
Female	7 (33.3)	7 (41.2)
Race		
African American	3 (14.3)	5 (29.4)
Asian	2 (9.5)	1 (5.9)
Caucasian	11 (52.4)	8 (47)
Hispanic	3 (14.3)	2 (11.8)
Other	2 (9.5)	1 (5.9)
Days intubated before tracheostomy	26 (22-29)	21 (19-24)

^aValues are presented as median (interquartile range) or No. (%).

HEMATOLOGY AND ONCOLOGY

FAVORABLE COVID-19 COURSE DESPITE SIGNIFICANT COMORBIDITIES IN A RUXOLITINIB-TREATED PATIENT WITH PRIMARY MYELOFIBROSIS

Koschmieder S, Jost E, Cornelissen C, Müller T, Schulze-Hagen M, Bickenbach J, Marx G, Kleines M, Marx N, Brümmendorf TH, Dreher M.. Eur J Haematol. 2020 Jun 27. doi: 10.1111/ejh.13480. Online ahead of print.

Level of Evidence: Other - Case Report

BLUF

This is a case of a 55-yo patient in Aachen, Germany with COVID-19 related pneumonia and pre-existing myeloproliferative neoplasm (MPN) treated with ruxolitinib (Table 1, Figure 1). The patient did not require vasopressor treatment or mechanical ventilation, and was discharged after 15 days despite having significant comorbidities, including chronic kidney disease, arterial hypertension, and obesity. The authors hypothesize that treatment with ruxolitinib for MPN may have contributed to a favorable clinical course of COVID-19.

SUMMARY

- The patient was diagnosed with calreticulin (CALR Del52)-mutant primary myelofibrosis 12 years ago and treated with ruxolitinib, initiated 15 months ago for constitutional symptoms and splenic pain.
- The patient reported coughing, dyspnea, fever, and chills eleven days before admission and tested positive for SARS-CoV-2 one day before admission.
- Treatment with ruxolitinib was continued since abrupt discontinuation of the treatment has been associated with severe cytokine storm and fatal acute respiratory distress syndrome (ARDS). No antibiotics were administered.
- Fifteen days after admission, and after three negative SARS-CoV-2 PCRs, the patient was discharged without the need for supplemental oxygen.
- Authors suggest that Janus-activated kinase (JAK) inhibition by ruxolitinib treatment may have facilitated a mild COVID-19 presentation in this patient.
- Furthermore, authors suggest that ruxolitinib treatment is not detrimental in patients with COVID-19, and further supports current recommendations to not discontinue ruxolitinib treatment in MPN patients who develop COVID-19.
- Moreover, ruxolitinib may potentially be effective in preventing "cytokine storm" among non-MPN, COVID-19 patients.

ABSTRACT

COVID-19 carries a high risk of severe disease course, particularly in patients with comorbidities. Therapy of severe COVID-19 infection has relied on supportive intensive care measures. More specific approaches including drugs that limit the detrimental "cytokine storm", such as Janus-activated kinase (JAK) inhibitors, are being discussed. Here, we report a compelling case of a 55-yo patient with proven COVID-19 pneumonia, who was taking the JAK1/2 inhibitor ruxolitinib in-label for co-existing primary myelofibrosis for 15 months prior to coronavirus infection. The patient had significant comorbidities, including chronic kidney disease, arterial hypertension, and obesity, and our previous cohort suggested that he was thus at high risk for acute respiratory distress syndrome (ARDS) and death from COVID-19. Since abrupt discontinuation of ruxolitinib may cause fatal cytokine storm and ARDS, ruxolitinib treatment was continued and was well tolerated, and the patient's condition remained stable, without the need for mechanical ventilation or vasopressors. The patient became negative for SARS-CoV-2 and was discharged home after 15 days. In conclusion, our report provides clinical evidence that ruxolitinib treatment is feasible and can be beneficial in patients with COVID-19 pneumonia, preventing cytokine storm and ARDS.

FIGURES

Table 1: Patient's clinical characteristics

Characteristics	
Age (ys)	55
Sex	male
Duration from first symptom to... (days)	
Hospitalization	10
Intensive care	10
Duration of... (days)	
Fever	17
Hospitalization	15
Therapy	
Intensive care	7
Mechanical ventilation	NA
ECMO	NA
Oxygen supplementation	12
Dialysis	NA

ECMO: Extracorporeal membrane oxygenation. NA: Not applicable.

Figure 1

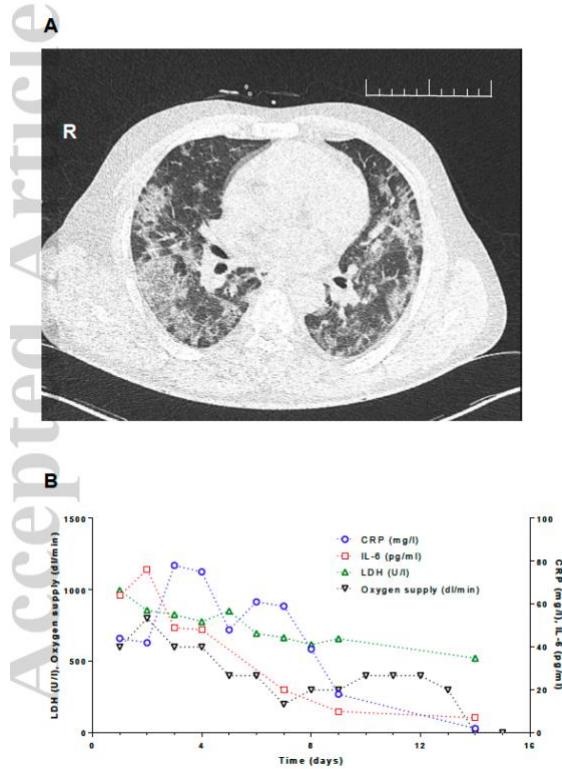


Figure 1: Chest CT scan at admission and clinical and laboratory parameters during the course of treatment. (A) The low dose computed tomography (CT) of the chest on the day of admission showed bilateral, predominantly peripheral "ground glass" opacities, focal consolidations and so-called "crazy paving", i.e. superimposed intra- and interlobular interstitial thickening. No pleural or pericardial effusion or coronary artery sclerosis was observed. No thoracic lymphadenopathy. In summary, the pattern of findings was categorized to be highly suggestive of COVID-19 associated pneumonia (COV-RADS 5). (B) Laboratory parameters lactate dehydrogenase, C-reactive protein (CRP), interleukin-6 (IL-6), and administered oxygen supply of the patient during the hospital stay (days after admission).

ADJUSTING PRACTICE DURING COVID-19

SURGICAL SUBSPECIALTIES

OTOLARYNGOLOGY

TELEMEDICINE ALGORITHM FOR THE MANAGEMENT OF DIZZY PATIENTS

Chari DA, Wu MJ, Crowson MG, Kozin ED, Rauch SD.. Otolaryngol Head Neck Surg. 2020 Jun 30;194599820935859. doi: 10.1177/0194599820935859. Online ahead of print.

Level of Evidence: 5 - Guidelines and Recommendations

BLUF

Otolaryngologists describe a telemedicine approach for general otolaryngologists on obtaining the history and physical examination of a patient presenting with dizziness (Figure 1). The authors stress the importance for taking a comprehensive history in telemedicine encounters since the virtual physical exam is limited to mainly mental status and ocular and facial nerve testing.

ABSTRACT

As a result of the COVID-19 pandemic, telemedicine has been thrust to the forefront of health care. Despite its inherent limitations, telemedicine offers many advantages to both patient and physician as an alternative to in-person evaluation of select patients. In the near term, telemedicine allows nonpandemic care to proceed while observing appropriate public health concerns to minimize the spread of pandemic pathogens. Thus, it behooves practitioners to use telemedicine consultations for common otolaryngology complaints. Assessment of the dizzy patient is well-suited to an algorithmic approach that can be adapted to a telemedicine setting. As best practices for telemedicine have yet to be defined, we present herein a practical approach to the history and limited physical examination of the dizzy patient in the telemedicine setting for the general otolaryngologist. Indeed, once the acute crisis has abated, we suspect that this approach will continue to be an effective way to manage dizzy patients.

FIGURES

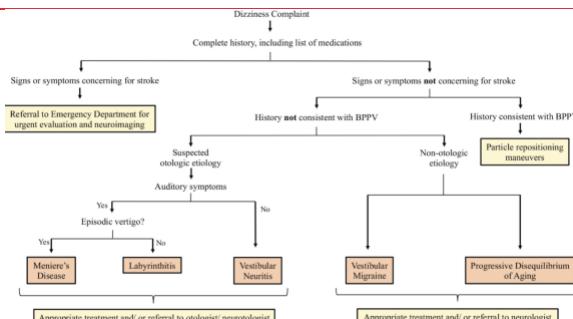


Figure 1. Algorithm for the management of patients with dizzy complaints.

MISCONCEPTIONS ABOUT NEGATIVE PRESSURE ROOMS AND THEIR IMPACT ABOARD USNS COMFORT IN NEW YORK CITY

Hill CJ, Capra GG, McDonald TP, Santiago GF, Radabaugh JP.. Otolaryngol Head Neck Surg. 2020 Jun 30;194599820938016. doi: 10.1177/0194599820938016. Online ahead of print.

Level of Evidence: Other - Guidelines and Recommendations

BLUF

Otolaryngologists from the Naval Medical Center, Virginia discussed appropriate air ventilation practices for limiting COVID-19 spread, which is especially relevant to otolaryngologists given high viral loads in their operative fields and frequent use of aerosol-generating procedures (AGPs) with possibility of viral aerosolization. Authors suggest that negative pressure alone does not provide sufficient infection control, and The Centers for Disease Control and Prevention (CDC) mandates that an

isolation room meets strict engineering guidelines to sufficiently reduce the spread of airborne infection (Table 1, 2). The authors suggest that a working knowledge of industrial hygiene grants physicians the ability to maximize safe practices by adapting clinical spaces.

ABSTRACT

The outbreak of novel coronavirus disease 2019 (COVID-19) has had a momentous impact on the field of otolaryngology due to the high number of aerosol-generating procedures involving the upper aerodigestive tract. These procedures bear significant risk to the provider and clinical environment due to the possibility of viral aerosolization. While significant attention has been appropriately paid to personal protective equipment during this pandemic, an understanding of industrial hygiene is also necessary for the safe delivery of health care to mitigate the risk of exposure to other patients and health care workers. We provide a review of air ventilation practices and their role in reducing pathogen spread. In addition, we share our experiences with effectively treating COVID-19-positive patients aboard the USNS Comfort through proper environment control measures.

FIGURES

Table 1. Engineering Controls Required for Isolation Rooms.		
1.	Maintain continuous negative pressure (-2.5 dPa) in relation to the air pressure in the corridor. Monitor periodically with manometer.	
2.	Ensure that rooms are well sealed.	
3.	Install self-closing devices on all isolation room doors.	
4.	Provide adequate ventilation to ensure $\geq 12 \text{ ACH}$ for new or renovated rooms and $\geq 6 \text{ ACH}$ for existing All rooms.	
5.	Direct exhaust air outside, away from intake and populated areas. If not practical, air may be recirculated after passing through HEPA filter.	

Abbreviations: ACH, air changes per hour; All, airborne infection isolation; HEPA, high-efficiency particulate air.

Table 2. Inverse Relationship Between Airflow and Time Required for Removal of Airborne Contaminants.

Air changes per hour	Time required for removal with 99% efficiency, min	Time required for removal with 99.9% efficiency, min
2	138	207
4	69	104
6	46	69
8	35	52
10	28	41
12	23	35
15	18	28
20	14	21
50	6	8

THORACIC SURGERY

THORACIC CANCER SURGERY DURING THE COVID-19 PANDEMIC: A CONSENSUS STATEMENT FROM THE THORACIC DOMAIN OF THE ASIAN SOCIETY FOR CARDIOVASCULAR AND THORACIC SURGERY

Jheon S, Ahmed AD, Fang VW, Jung W, Khan AZ, Lee JM, Sihoe AD, Thongcharoen P, Tsuboi M, Turna A, Nakajima J.. Asian Cardiovasc Thorac Ann. 2020 Jul 1:218492320940162. doi: 10.1177/0218492320940162. Online ahead of print.

Level of Evidence: Other - Guidelines and Recommendations

BLUF

Twenty-six thoracic surgeons, all panel members of The Thoracic Domain of the Asian Society for Cardiovascular and Thoracic Surgery (ASCVTS), developed a series of consensus recommendations through the Delphi process, using two surveys taken April 11–12, 2020 and April 14–18, 2020. The consensus recommendations pertain to the operation of thoracic surgical units in areas affected by COVID-19 outbreaks and include several precautions and provisions for providing thoracic cancer surgery services during the pandemic (Table 4). A key recommendation is for the deferral of all elective surgeries, though the authors note that all procedures for solid tumors should proceed as planned regardless of stage and also recognize that cancer management should ultimately be personalized and may be fluid under certain circumstances.

ABSTRACT

OBJECTIVES: Healthcare resources have been mobilized to combat the COVID-19 pandemic of 2020. The Thoracic Domain of the Asian Society for Cardiovascular and Thoracic Surgery reports a consensus statement on the provision of thoracic cancer surgery during this pandemic. METHODS: A Thoracic Experts Panel was convened by the Society. A consensus on the provision, safety, and setting of thoracic cancer surgery during the pandemic was obtained through a Delphi process.

RESULTS: Responses were received from 26 panel members (96% response rate) from 10 regions across Asia. The Society recommended that elective thoracic cancer surgery services may need to be reduced or postponed if medical resources were needed for COVID-19 patients, especially intensive care unit beds and ventilators. However, thoracic cancer surgery should proceed as normal for all solid tumors, without restrictions based on disease stage, availability of non-surgical treatment options, or patient condition (unless there is a high likelihood of postoperative intensive care unit stay). Aerosol-forming procedures should be avoided intra- and perioperatively. The surgical approach does not make a difference in terms of safety. Services for thoracic cancer patients should be offered only in hospitals that maintain isolation wards for patients with confirmed or suspected COVID-19. CONCLUSIONS: Services for patients with thoracic cancer should be maintained during the COVID-19 pandemic. The position of the Society is that thoracic surgeons have a responsibility to perform good surgical management of thoracic cancer during the pandemic, to advocate for patients' rights to receive it, and to safeguard patients and staff from infection.

FIGURES

Recommendation	Consensus
Provision of thoracic cancer surgery services	
Proceed with all thoracic cancer surgery but with reduced operating room sessions per week	Recommended
Do not operate on any patient currently with confirmed or suspected COVID-19 (contact history, symptoms)	Recommended
Proceed with surgery in patients with solid (non-GGO) tumors	Weakly recommended
Proceed with all thoracic cancer surgery, except when there is high likelihood of ICU admission/ prolonged hospital stay	Recommended
Non-surgical treatment options should not affect decision for offering surgery	Recommended
Elective surgery should be rejected/deferred if there is a need to reserve ICU beds or ventilators for COVID-19 patients	Highly recommended
Elective surgery should be rejected/deferred if there is a need to reserve PPE for staff treating COVID-19 patients	Recommended
Elective surgery should be rejected/deferred if there is a need to allocate doctors and nurses to manage COVID-19 patients	Recommended
Safety	
Choice of surgical approach makes no difference when performing thoracic cancer surgery for patients with confirmed/suspected COVID-19	Recommended
Bronchoscopy (fiberoptic/crigg) should be avoided intraoperatively	Highly recommended
Cross-fieldlet ventilation should be avoided intraoperatively	Recommended
Sputum suction via endotracheal tubes should be avoided intraoperatively	Recommended
Tracheostomy/minitracheostomy should be avoided intraoperatively	Recommended
Bronchoscopy (including EBUS and ENB) should be avoided perioperatively	Recommended
Nasopharyngeal suction should be avoided postoperatively	Recommended
Discharge home with chest drain in situ should be avoided postoperatively	Recommended
Setting for thoracic cancer surgery services	
Thoracic cancer surgery should be performed only in hospitals with separate, designated ICU and isolation wards for patients with confirmed/suspected COVID-19	Recommended
Preoperative investigations and postoperative follow-up should only be offered in hospitals with separate, designated isolation wards for patients with confirmed/suspected COVID-19	Recommended

Table 4. Recommendations of the Asian Society for Cardiovascular and Thoracic Surgery regarding thoracic cancer surgery services during the COVID-19 pandemic.

OBGYN

HOW COVID MAY IMPROVE CARE: RETHINKING CERVICAL CANCER PREVENTION

Feldman S, Haas JS.. J Natl Cancer Inst. 2020 Jul 1:djaa089. doi: 10.1093/jnci/djaa089. Online ahead of print.

Level of Evidence: Other - Expert Opinion

BLUF

Physicians at Harvard Medical School, Boston discuss changes in cervical cancer screening and prevention during the COVID-19 pandemic, worrying that delayed care may lead to increased morbidity and mortality. The authors consider innovations such as vaginal self-testing for HPV, specialized counseling and education via telehealth visits, and education on importance of all vaccinations (i.e. HPV, COVID-19) as areas of opportunity for improved patient care. They hope to utilize the circumstances of this pandemic for overall advancement of the healthcare system through reflection and innovation of new patient care strategies.

ABSTRACT

These past months of the COVID pandemic have given us ample opportunity to reflect on the US health care system. Despite overwhelming tragedy, it is an opportunity for us to learn and to change. As we postpone routine visits because of the pandemic, we worry about risks for patients who delay cancer screening. We use cervical cancer screening and prevention as an example of how we can use some "lessons learned" from the pandemic to prevent "collateral losses," such as an increase in cancers. COVID-related health system changes, like the more rapid evaluation of diagnostic tests and vaccines, the transition to

compensated virtual care for most counseling and education visits, and broadened access to home services all offer potential benefits to the delivery of cervical cancer screening and prevention. While we detail the case for cervical cancer prevention, many of the issues discussed are generalizable to other preventative measures. It would be a tragedy if the morbidity and mortality of COVID is multiplied because of additional suffering caused by delayed or deferred cancer screening and diagnostic evaluation-but maybe with creativity and reflection, we can use this pandemic to improve care.

PSYCHIATRY

SCREENING FOR SARS-COV-2 INFECTION WITHIN A PSYCHIATRIC HOSPITAL AND CONSIDERATIONS FOR LIMITING TRANSMISSION WITHIN RESIDENTIAL PSYCHIATRIC FACILITIES - WYOMING, 2020

Callaghan AW, Chard AN, Arnold P, Loveland C, Hull N, Saraiya M, Saydah S, Dumont W, Frakes LG, Johnson D, Peltier R, Van Houten C, Trujillo AA, Moore J, Rose DA, Honein MA, Carrington D, Harrist A, Hills SL.. MMWR Morb Mortal Wkly Rep. 2020 Jul 3;69(26):825-829. doi: 10.15585/mmwr.mm6926a4.

Level of Evidence: 3 - Local non-random sample

BLUF

A point prevalence survey conducted at Wyoming's state psychiatric hospital on 1 May 2020 assessed the effectiveness of enhanced COVID-19 infection prevention and control (IPC) measures (screening, testing, patient isolation/management, use of modified face coverings) that were implemented following admission of two SARS-CoV-2 positive patients on 16 April 2020. Authors surveyed 61% of patients (n=46) and 61% of health care personnel (HCP; n=171) via questionnaire (Table 1) and collected nasopharyngeal swabs from participants to test for SARS-CoV-2 RNA by reverse transcription-polymerase chain reaction (RT-PCR). They found that 88% of HCP reported providing direct care to the patients and 57% reported working across multiple units in the previous 2 weeks. Authors also report that all RT-PCR tests were negative, suggesting that expanded IPC strategies may have been effective in preventing viral spread. Authors conclude that adapting standard IPC procedures may be necessary to prevent transmission among patients and HCP in psychiatric facilities given their unique challenges (Table 2), which was shown to be effective in the present study.

ABSTRACT

In the United States, approximately 180,000 patients receive mental health services each day at approximately 4,000 inpatient and residential psychiatric facilities (1). SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19), can spread rapidly within congregate residential settings (2-4), including psychiatric facilities. On April 13, 2020, two patients were transferred to Wyoming's state psychiatric hospital from a private psychiatric hospital that had confirmed COVID-19 cases among its residents and staff members (5). Although both patients were asymptomatic at the time of transfer and one had a negative test result for SARS-CoV-2 at the originating facility, they were both isolated and received testing upon arrival at the state facility. On April 16, 2020, the test results indicated that both patients had SARS-CoV-2 infection. In response, the state hospital implemented expanded COVID-19 infection prevention and control (IPC) procedures (e.g., enhanced screening, testing, and management of new patient admissions) and adapted some standard IPC measures to facilitate implementation within the psychiatric patient population (e.g., use of modified face coverings). To assess the likely effectiveness of these procedures and determine SARS-CoV-2 infection prevalence among patients and health care personnel (HCP) (6) at the state hospital, a point prevalence survey was conducted. On May 1, 2020, 18 days after the patients' arrival, 46 (61%) of 76 patients and 171 (61%) of 282 HCP had nasopharyngeal swabs collected and tested for SARS-CoV-2 RNA by reverse transcription-polymerase chain reaction. All patients and HCP who received testing had negative test results, suggesting that the hospital's expanded IPC strategies might have been effective in preventing the introduction and spread of SARS-CoV-2 infection within the facility. In congregate residential settings, prompt identification of COVID-19 cases and application of strong IPC procedures are critical to ensuring the protection of other patients and staff members. Although standard guidance exists for other congregate facilities (7) and for HCP in general (8), modifications and nonstandard solutions might be needed to account for the specific needs of psychiatric facilities, their patients, and staff members.

FIGURES

TABLE 1. Characteristics of patients and health care personnel (HCP) who participated in the point prevalence survey at a state psychiatric hospital — Wyoming, May 2020

Patient characteristic	Adult psychiatric	Medical geriatric psychiatric	Criminal justice	Total patients
No. participating/total no.	21/31	16/21	9/24	46/76
Male, no. (%)	8 (38)	4 (25)	6 (67)	18 (39)
Median age, yrs (IQR)	48 (38–61)	62 (57–66)	42 (32–59)	57 (41–63)
Median length of admission, days (IQR)	107 (76–176)	320 (121–735)	150 (73–228)	150 (86–381)
HCP characteristic				
Clinical care			Housekeeping	Transport/Security
No. participating/total no.	13/20	14/20	2/20	17/20*
Male, no. (%)	37 (77)	0 (0)	13 (65)	50 (59)
Median age, yrs (IQR)	41 (32–54)	55 (43–57)	46 (34–53)	43 (32–55)
Provided direct patient care, no. (%) [†]	132 (96)	2 (14)	18 (90)	151 (88)
Worked at one health care facility within previous 2 weeks, no. (%)	7 (5)	0 (0)	1 (5)	8 (5)
Worked on multiple units at the state hospital within previous 2 weeks, no. (%)	72 (53)	10 (71)	17 (85)	98 (57)

Abbreviations: IQR = interquartile range.
* One HCP staff member was excluded because the sample arrived at the testing laboratory without a label.
[†] As reported by HCP; at times housekeeping, transportation, and security staff members might provide nonclinical direct patient care, such as assisting the patients to move around the facility or intervening if a patient becomes violent.

TABLE 2. Infection prevention, control, and other considerations based on observations at psychiatric facilities during the COVID-19 pandemic—Wyoming, May 2020

Group/Process	Challenges to effective COVID-19 prevention and control	Possible solutions
Patients		
Admission	Admissions from facilities at higher risk for SARS-CoV-2 transmission (e.g., homeless shelters, group homes, and correctional facilities).	Test newly admitted patients to identify any persons with asymptomatic infection and defer migration to regular wards until results are received. If result is positive, keep patient isolated; if result is negative, conduct routine symptom screening on regular ward.
Screening	Uncooperative/violent behavior by some patients are being a barrier for appropriate or timely SARS-CoV-2 infection.	Educate patients to raise awareness of the need for screening and testing, and to avoid transmission and isolation.
Cohorting	Logistical challenge to segregate according to age, gender, treatment needs, and potential for violence in addition to cohorting based on COVID-19 case status.	Implement rigorous infection control measures to prevent transmission between patients. Implement strict cohorting in addition to the normal necessary segregation of patients. If transmission occurs, isolate patients in single rooms, or in rooms with other COVID-19 patients based on patient needs and available resources.
Social distancing	Psychiatric treatment often requires close interaction and cannot be canceled or delayed.	Consider smaller group sessions or one-on-one therapy with 6-foot distancing, universal use of face coverings, and more frequent decontamination of surfaces.
Use of face coverings for source control	Face coverings unsuitable for patient use or patient noncompliant with use.	Consider modifications to settings, modified methods of securing face coverings, or the use of facility-approved items as face coverings when possible and accepted by the patient.
Exposure to cleaning products and disinfectants	Risks associated with patient behaviors (e.g., licking surfaces, attempts to ingest products if accessible).	Have staff members follow instructions to product labels for safe use. Have staff members use PPE when interacting with unpartnered persons such as patients; have staff members dispense individual portions of hand sanitizer directly to patients as needed.
Close connections with other high-risk facilities	Regular transfers from facilities at higher risk for SARS-CoV-2 transmission (e.g., homeless shelters, group homes, and correctional facilities).	Develop contingency and surge plans that support the needs of all higher-risk facilities and address issues such as integrated testing strategies, expanded screening approaches, and community surveillance.
Staff members		
Physical strain	Time-consuming, frequent wellbeing checks; need for physical restraint of violent/uncooperative patients.	Plan for additional or surge workforce capacity; consider flexible leave policies to account for added strain; make provisions for any staff member at higher risk of severe outcomes from COVID-19.
Emotional strain	Possible high HCP turnover; potential stigma of working in a psychiatric facility with active SARS-CoV-2 transmission.	Plan for additional or surge workforce capacity; develop a communications plan to address stigma.
Risk of exposure for clinical care staff members	Patient behavior might increase risk of SARS-CoV-2 exposure (e.g., spitting, biting, thrashing, or intentionally removing PPE).	Use modified PPE to allow unrestricted movement and reduce risks of transmission. Encourage staff members working with violent and nonviolent patients (e.g., goggles instead of glasses or face shields, respirators instead of surgical masks, or Tyvek suits instead of gowns).
Risk of exposure for nonclinical care staff members	Security staff members constantly present on some wards, might be first to respond to a patient in a violent situation, increasing potential for high-risk exposure; similar risks for transportation staff members who interact with patients during transfer.	Use modified PPE to allow unrestricted movement and provide access to personal protective equipment (e.g., goggles instead of glasses or face shields, respirators instead of surgical masks, or Tyvek suits instead of gowns).
Buildings/Wards		
Social distancing	Open patient wards and -rooms to facilitate patient observation; many spaces (including bathrooms) are crowded.	Control and monitor access to communal areas by symptomatic patients; implement enhanced disinfection practices.
Cohorting	Converting single rooms to double occupancy or moving patients to different wards for disease cohorting might be problematic given patients' different psychiatric needs.	Utilize other available structures or facilities when possible.
Clinical case management	Units and patient rooms often not set up to provide multifaceted clinical care for safety reasons; rooms often do not include electric outlets to run medical equipment.	Plan for transfer of patients to acute care hospitals as needed.

Abbreviations: COVID-19 = coronavirus disease 2019; HCP = health care personnel; PPE = personal protective equipment.

R&D: DIAGNOSIS & TREATMENTS

CURRENT DIAGNOSTICS

DETECTING SARS-COV-2 RNA IN CONJUNCTIVAL SECRETIONS: IS IT A VALUABLE DIAGNOSTIC METHOD OF COVID-19?

Güemes-Villahoz N, Burgos-Blasco B, Vilela AA, Arriola-Villalobos P, Luna CMR, Sardiña RC, Delgado-Iribarren A, García-Feijoó J.. *J Med Virol.* 2020 Jun 24. doi: 10.1002/jmv.26219. Online ahead of print.

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

BLUF

A cross-sectional study in Spain investigated the presence of SARS-CoV-2 on conjunctival swabs of 36 COVID-19 patients (n=18 with conjunctivitis, n=18 without conjunctivitis) and found the same rate of positive results for each group (Table 1). Based on this they believe ocular samples provide limited diagnostic value and recommend standardized methods of sample collection in future research.

ABSTRACT

PURPOSE: To evaluate the presence of viral RNA of SARS-CoV-2 in conjunctival swab specimen of COVID-19 patients with and without conjunctivitis to establish the diagnostic value of reverse transcription-polymerase chain reaction (RT-PCR) in each case and to describe its clinical characteristics. **METHODS:** Cross-sectional study conducted at the Hospital Clínico San Carlos of Madrid, Spain. 36 subjects from the COVID admission unit with laboratory-confirmed SARS-CoV-2 infection were included. Conjunctival swabs were collected from 18 patients with conjunctivitis and 18 patients without conjunctivitis. RT-PCR was performed. **RESULTS:** Conjunctival swab was collected from both eyes of 36 patients (72 eyes), detecting SARS-CoV-2 RNA in conjunctival swab of two patients (5.5%). Among the 18 patients with conjunctivitis, only 1 of them (5.5%) showed positive results. Likewise, SARS-CoV-2 RNA was detected in 1 patient without conjunctivitis (5.5%). The mean age of the 36 patients was 67.9 years (range 28-92 years) and the male-to-female ratio was 0.44 (16:20). The mean days since onset of COVID-19 symptoms until conjunctivitis manifestation was 8 (range 1-24 days). The mean duration of the conjunctivitis was 3 days (range 1-7 days). **CONCLUSION:** SARS-CoV-2 RNA may be detected in conjunctival swabs of both patients with and without conjunctivitis. Our study revealed the same rate of positive results amongst the group with and without conjunctivitis, suggesting that detecting SARS-CoV-2 in ocular fluids is not conditioned on the presence of conjunctivitis. The presence of SARS-CoV-2 RNA in ocular samples highlights the role of the eye as a possible route of transmission of the disease. This article is protected by copyright. All rights reserved.

FIGURES

	With conjunctivitis	Without conjunctivitis
Sex		
Male (%)	39	50
Female (%)	61	50
Age (years)	$70,3 \pm 21,6$	$65,4 \pm 18,9$
Clinical severity		

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Mild (%)	50	44
Moderate (%)	33	33
Severe (%)	17	22
Pneumonia (%)	67	72

Table 1 Clinical characteristics among patients with and without conjunctivitis.

DEVELOPMENTS IN DIAGNOSTICS

EVALUATION OF NOVEL CORONAVIRUS DISEASE (COVID-19) USING QUANTITATIVE LUNG CT AND CLINICAL DATA: PREDICTION OF SHORT-TERM OUTCOME

Matos J, Paparo F, Mussetto I, Bacigalupo L, Veneziano A, Perugini Bernardi S, Biscaldi E, Melani E, Antonucci G, Cremonesi P, Lattuada M, Pilotto A, Pontali E, Rollandi GA.. Eur Radiol Exp. 2020 Jun 26;4(1):39. doi: 10.1186/s41747-020-00167-0.

Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

Using classification algorithms, authors from Italy prospectively enrolled 106 patients (median age 63.5 years) from March 1st to March 22nd with positive CT finding and RT-PCR for SARS-CoV-2 to assess whether clinical data (CRP, % lymphocytes, and CT scan) predict clinical outcomes in COVID-19 patients. It was found that the volume of disease observed on CT lung imaging was a predictor of short-term patient outcome and that CRP values could accurately predict the volume of disease ($p<0.001$). Thus, the authors suggest that these clinical markers can be used for patient risk assessment when RT-PCR results cannot be quickly obtained.

ABSTRACT

BACKGROUND: Computed tomography (CT) enables quantification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, helping in outcome prediction. **METHODS:** From 1 to 22 March 2020, patients with pneumonia symptoms, positive lung CT scan, and confirmed SARS-CoV-2 on reverse transcription-polymerase chain reaction (RT-PCR) were consecutively enrolled. Clinical data was collected. Outcome was defined as favourable or adverse (i.e., need for mechanical ventilation or death) and registered over a period of 10 days following CT. Volume of disease (VoD) on CT was calculated semi-automatically. Multiple linear regression was used to predict VoD by clinical/laboratory data. To predict outcome, important features were selected using *a priori* analysis and subsequently used to train 4 different models. **RESULTS:** A total of 106 consecutive patients were enrolled (median age 63.5 years, range 26–95 years; 41/106 women, 38.7%). Median

duration of symptoms and C-reactive protein (CRP) was 5 days (range 1-30) and 4.94 mg/L (range 0.1-28.3), respectively. Median VoD was 249.5 cm³ (range 9.9-1505) and was predicted by lymphocyte percentage ($p = 0.008$) and CRP ($p < 0.001$). Important variables for outcome prediction included CRP (area under the curve [AUC] 0.77), VoD (AUC 0.75), age (AUC 0.72), lymphocyte percentage (AUC 0.70), coronary calcification (AUC 0.68), and presence of comorbidities (AUC 0.66). Support vector machine had the best performance in outcome prediction, yielding an AUC of 0.92. CONCLUSIONS: Measuring the VoD using a simple CT post-processing tool estimates SARS-CoV-2 burden. CT and clinical data together enable accurate prediction of short-term clinical outcome.

FIGURES

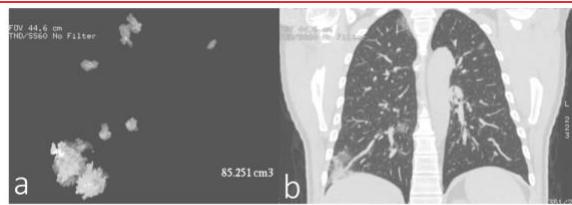


Fig. 2 Example of severe acute respiratory syndrome coronavirus 2 lung disease segmentation. **a** Maximum intensity projection coronal image shows segmented lung opacities and the volume provided in cubic centimeters. **b** Corresponding coronal computed tomography image

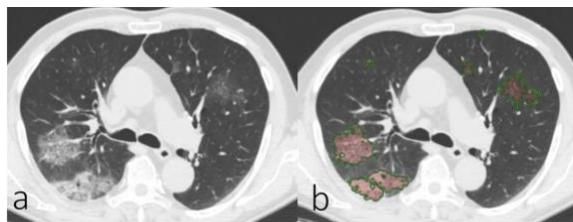


Fig. 3 Example of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) lung disease segmentation. Typical SARS-CoV-2 pneumonia with lung opacities before **(a)** and after **(b)** semi-automatic segmentation

Table 1 Demographic, clinical, and laboratory data of the study population

Demographics	
Age (years; median, range)	63.5 (26-95)
Male (number, percentage)	65/106 (61.3)
Female (number, percentage)	41/106 (38.7)
Clinical information	
No comorbidity (number, percentage)	66/106 (62.3)
Presence of ≥ 1 comorbidity	40/106 (37.7)
Duration of symptoms at computed tomography (days; median, range)	5 (1-30)
Laboratory information	
White blood cell count ($10^9/L$) (median, range)	5.7 (1.9-29.7)
Lymphocyte (%) (median, range)	18.8 (2.2-53.0)
C-reactive protein (mg/L) (median, range)	4.94 (0.1-28.3)
Admitted/discharged from emergency department	
Admitted	97/106 (91.5%)
Discharged from the emergency department	9/106 (8.5%)
Outcome	
Favourable	64/106 (60.4%)
Adverse	42/106 (39.6%)
Outcome subgroups	
Need for mechanical ventilation	17/42 (40.5%)
Death	25/42 (59.5%)

DEVELOPMENT AND MULTICENTER PERFORMANCE EVALUATION OF FULLY AUTOMATED SARS-COV-2 IGM AND IGG IMMUNOASSAYS

Qian C, Zhou M, Cheng F, Lin X, Gong Y, Xie X, Li P, Li Z, Zhang P, Liu Z, Hu F, Wang Y, Li Q, Zhu Y, Duan G, Xing Y, Song H, Xu W, Liu BF, Xia F.. Clin Chem Lab Med. 2020 Jul 1:/j/cclm.ahead-of-print/cclm-2020-0548/cclm-2020-0548.xml. doi: 10.1515/cclm-2020-0548. Online ahead of print.

Level of Evidence: 4 - Case-control studies, or “poor or non-independent reference standard

BLUF

Automated chemiluminescent immunoassays (CLIA) for SARS-CoV-2 have been developed in China to detect human IgM and IgG antibodies in human serum, with high specificity (Table 3) and sensitivity (Table 4). This system was developed and evaluated at 10 hospitals (972 patients and 586 community donor samples), with detection of both IgM and IgG measured by comparing confirmed cases with PCR, adding another potential diagnostic for monitoring COVID-19 infection that the authors believe can be more accurate than current nucleic acid testing.

ABSTRACT

Objectives The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly spread globally. The laboratory diagnosis of SARS-CoV-2 infection has relied on nucleic acid testing; however, it has some limitations, such as low throughput and high rates of false negatives. Tests of higher sensitivity are needed to effectively identify infected patients.

Methods This study has developed fully automated chemiluminescent immunoassays to determine IgM and IgG antibodies to SARS-CoV-2 in human serum. The assay performance has been evaluated at 10 hospitals. Clinical specificity was evaluated by measuring 972 hospitalized patients and 586 donors of a normal population. Clinical sensitivity was assessed on 513 confirmed cases of SARS-CoV-2 by RT-PCR. **Results** The assays demonstrated satisfied assay precision with coefficient of variation of less than 4.45%. Inactivation of specimen did not affect assay measurement. SARS-CoV-2 IgM showed clinical specificity of 97.33 and 99.49% for hospitalized patients and the normal population respectively, and SARS-CoV-2 IgG showed clinical specificity of 97.43 and 99.15% respectively. SARS-CoV-2 IgM showed clinical sensitivity of 82.54, 92.93, and 84.62% before 7 days, 7-14 days, and after 14 days respectively, since onset of symptoms, and SARS-CoV-2 IgG showed clinical sensitivity of 80.95, 97.98, and 99.15% respectively at the same time points above. **Conclusions** We have developed fully automated immunoassays for detecting SARS-CoV-2 IgM and IgG antibodies in human serum. The assays demonstrated high clinical specificity and sensitivity, and add great value to nucleic acid testing in fighting against the global pandemic of the SARS-CoV-2 infection.

FIGURES

Sample Number	SARS-CoV-2 IgM			SARS-CoV-2 IgG			
	Negative	Positive	Clinical Specificity	Negative	Positive	Clinical Specificity	
Hospitalized Patients	972	946	26	97.33%	947	25	97.43%
Normal Population	586	583	3	99.49%	581	5	99.15%

Table 3. Clinical specificity of SARS-CoV-2 IgM and SARS-CoV-2 IgG

Sample Number	SARS-CoV-2 IgM			SARS-CoV-2 IgG			
	Negative	Positive	Clinical Sensitivity	Negative	Positive	Clinical Sensitivity	
Confirmed SARS-CoV-2 infection (RT-PCR positive)	503	71	432	85.88%	17	486	96.62%
Suspected SARS-CoV-2 infection (RT-PCR negative)	52	14	38	73.08%	7	45	86.54%

Table 4. Clinical sensitivity of SARS-CoV-2 IgM and SARS-CoV-2 IgG

ANTIBODY TESTING FOR COVID-19

Grenache DG, Sever C, Mathur G, Mathur S.. Am J Clin Pathol. 2020 Jun 24:aqaa110. doi: 10.1093/ajcp/aqaa110. Online ahead of print.

Level of Evidence: Other - Expert Opinion

BLUF

Authors from TriCore Reference Laboratories responded to a recent editorial (Mathur et al, 2020) about antibody testing for COVID-19 that was given FDA emergency use authorization in April 2020. They critique the calculation of test sensitivity using the total of all samples independent of timing as opposed to in relation to day of onset or diagnosis. Included in this

correspondence, Mathur et al respond with their explanation for why the average of all samples was used (see summary). These critiques should be considered when reading the original article and evaluating sensitivity of the antibody test.

SUMMARY

In this correspondence, the main critique is regarding the clinical sensitivity of the tests - the authors from Tricore believe that it is misleading to calculate sensitivity using the total of all samples tested regardless of timing (as Mathur et al did). The Tricore authors believe onset of infection or diagnosis should be considered. Mathur et al respond to the critique with three main arguments for using the average of all samples tested: "(1) there is no uniformity in the data submitted to the FDA by test manufacturers[sic]; (2) the table would have been too lengthy if we had split out sensitivity and specificity for each cohort tested for each manufacturer; and (3) clinically the patients most likely will be tested irrespective of days post infection or start of the symptoms." These critiques and the correspondence between these authors should be considered when looking at the original article and the sensitivity of the antibody test.

DEVELOPMENTS IN TREATMENTS

USE OF ANAKINRA TO PREVENT MECHANICAL VENTILATION IN SEVERE COVID-19: A CASE SERIES

Navarro-Millán I, Sattui SE, Lakhapal A, Zisa D, Siegel CH, Crow MK.. Arthritis Rheumatol. 2020 Jun 30. doi: 10.1002/art.41422. Online ahead of print.

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

BLUF

This retrospective case series conducted at New York Presbyterian Hospital identified patients with COVID-19, features of cytokine storm syndrome, and acute hypoxic respiratory failure (AHRF), and evaluated the efficacy of anakinra in preventing mechanical ventilation in these patients. Seven of these patients who received anakinra within 36 hours did not require mechanical ventilation (MV). Four who received anakinra after 4 days of AHRF onset required MV and of those, three were extubated and one died (Table 2). The authors urge investigators to consider clinical trials to study the safety and efficacy of anakinra in patients with COVID-19.

ABSTRACT

OBJECTIVE: To report the clinical experience with anakinra for preventing mechanical ventilation (MV) in patients with COVID-19, features of cytokine storm syndrome (CSS), and acute hypoxic respiratory failure (AHRF). **METHODS:** In this retrospective case series, patients must have had SARS-CoV-2, fever, ferritin >1,000 ng/mL with one additional laboratory marker of hyperinflammation, and AHRF. AHRF was defined as requiring 15L of supplemental oxygen via non-rebreather mask combined with 6L nasal cannula or use of >=95% oxygen by high flow nasal cannula. We excluded patients with suspicion for bacterial infection or on immunosuppressants. Subcutaneous anakinra was initiated at 100 mg q6 hours and gradually tapered off completely. Primary outcome was prevention of MV. **RESULTS:** Eleven of 14 patients meeting criteria received anakinra for a maximum of 19 days. Seven of those who initiated anakinra <=36 hours after onset of AHRF did not require MV, and all were discharged home. Four patients who started anakinra >=4 days after onset of AHRF required MV. Of those, 3 patients were extubated (2 discharged home, 1 remains hospitalized) and 1 died. All 3 patients who met criteria but did not receive anakinra required MV. Two were extubated (1 discharged and 1 remains hospitalized) and 1 remains on MV. **CONCLUSIONS:** Our data suggest that anakinra could be beneficial in COVID-19 patients with evidence of CSS when initiated early after onset of AHRF. Our patient selection and treatment approach should be considered for investigation in a clinical trial to determine the safety and efficacy of anakinra in patients with COVID-19 and features of CSS.

FIGURES

Table 2: Concomitant Therapies and Clinical Outcomes in COVID-19 Patients Treated with Anakinra

Patient ID	Concomitant medications	Time from initiation of maximum supplemental O-(NFB 10-15L + NC 6L or HFNc) to initiation of Anakinra	Anakinra Dose/Duration	Days on Anakinra	Current clinical status and observation	Adverse reactions while on anakinra
Patients treated with anakinra						
1	None	18 hours	≤ 100 mg SQ daily on day 8, discontinued on day 9	9	Discharged from hospital, no limitation on activities (1).	None
2	None	36 hours	≤ 100 mg SQ q24h on day 2, ≤ 100 mg SQ q24h on day 4, ≤ 100 mg SQ q24h on day 10, ≤ 100 mg SQ daily on day 13	19	Discharged from hospital, no limitation on activities (1). Received anakinra 100 mg daily for 5 days as outpatient.	Elevation of AST/ALT (also on scheduled asteptremepat), injection site reaction on last 2 days of treatment.
3	Methylprednisolone 20 mg q24h x 4 days prior to starting anakinra, tapered after 10 days (total 14 days)	24 hours	≤ 100 mg SQ q24h on day 3, ≤ 100 mg SQ q24h on day 5, ≤ 100 mg SQ daily day 8, discontinued day 12	12	Discharged from hospital, no limitation on activities (1).	None
4	Methylprednisolone 40 mg q12h x 3 days prior to starting anakinra (total 3 days)	4 days	≤ 100 mg SQ q24h on day 4, ≤ 100 mg SQ q24h on day 6, discontinued day 12	12	Hospitalized without oxygen support (3). Required MV for 19 days.	Bacterial infection
5	Methylprednisolone 20 mg q12h x 3 days prior to starting anakinra (total 3 days)	4 days	Discontinued on day 2	2	Death (R): Anakinra discontinued after 8 doses due to bacterial infection*	Bacterial infection*
6	Methylprednisolone 30 mg q12h x 4 days prior to starting anakinra (total 4 days)	24 hours	≤ 100 mg SQ q24h on day 3, ≤ 100 mg SQ q24h on day 5, ≤ 100 mg SQ daily day 11, discontinued day 12	12	Discharged from hospital, no limitation on activities (1).	Elevation of AST/ALT and leukopenia
7	Methylprednisolone 50 mg q12h x 4 days prior to starting anakinra (total 5 days)	7 days	≤ 100 mg SQ q24h on day 5, ≤ 100 mg SQ q24h on day 7, ≤ 100 mg SQ q24h day 9, discontinued day 9	9	Discharged from hospital, with limitation on activities (2). Hospitalized, required invasive MV for 16 days. Initiated after 1 dose of anakinra.	Bacterial infection
8	Methylprednisolone 40 mg q12h x 1 day, tapered during following 7 days (while on anakinra)	18 hours	≤ 100 mg SQ q24h on day 3, ≤ 100 mg SQ q24h on day 15, ≤ 100 mg SQ daily day 16, discontinued day 17	17	Discharged from hospital, with limitation on activities (2).	None
9	Methylprednisolone 40 mg daily x 5 days (2 weeks prior to anakinra), then methylprednisolone 40 mg q12h x 3 days (simultaneous with the first 5 days of anakinra)	4 days after extubation	≤ 100 mg SQ q24h on day 4, ≤ 100 mg SQ q24h on day 5, ≤ 100 mg SQ q24h on day 12, discontinued day 17	17	Discharged from hospital, with limitation on activities (2). Required MV for 6 days. Met criteria for CRSS before and after extubation but consulted for anakinra treatment only after extubation.	None
10	Methylprednisolone 40 q12h x 1 day (prior to anakinra)	24 hours	≤ 100 mg SQ q24h on day 6, discontinued on day 7.	7	Discharged from hospital, no limitation on activities (1). Received MV for 16 days. Patient was intubated on day 1 of extubation.	High suspicion for bacterial infection.
11	None	24 hours	≤ 100 mg SQ q24h on day 2, discontinued day 4	4	Discharged from hospital, no limitation on activities (1). No anakinra on discharge.	Elevation of AST/ALT High suspicion for bacterial superinfection.
Patients not treated with anakinra but meeting criteria						
12	Received tocilizumab and glucocorticoids	Not applicable	Anakinra not available in the hospital	0	Hospitalized, requiring supplemental 6L NC oxygen (4). Q saturation 98%. Required MV for 15 days. Met criteria for CRSS again for 8 more days. Not extubated.	Not applicable
13	Received sarilumab and glucocorticoids	Not applicable	Anakinra not available in the hospital	0	Discharged from hospital, no limitation on activities (1).	Not applicable
14	Received sarilumab and glucocorticoids	Not applicable	Patient declined anakinra	0	Hospitalized requiring invasive MV with tracheostomy (8) 4 th days on MV as of June 2, 2020.	Not applicable

All except patients 8 and 11 received hydroxychloroquine. All patients were off anakinra by the end of the case series.

*Patient's blood culture were drawn before anakinra was initiated and results were pending when the medication was started. Once the results were positive, we discontinued anakinra.

^aClinical status graded on 9-point ordinal scale suggested by the World Health Organization.

AN IN VITRO MICRONEUTRALIZATION ASSAY FOR SARS-COV-2 SEROLOGY AND DRUG SCREENING

Amanat F, White KM, Miorin L, Strohmeier S, McMahon M, Meade P, Liu WC, Albrecht RA, Simon V, Martinez-Sobrido L, Moran T, García-Sastre A, Krammer F. Curr Protoc Microbiol. 2020 Sep;58(1):e108. doi: 10.1002/cpmc.108.

Level of Evidence: 5 - Mechanism-based reasoning

BLUF

In this publication, a group of researchers affiliated with Icahn School of Medicine describe protocols for microneutralization and antiviral assays that they state can be used to evaluate inhibitory ability of antibodies or compounds against the SARS-CoV-2 virus in vitro (Figure 3). They argue that current assays have significant limitations including lower throughput (e.g. less efficiency) and an inability to assess inhibition quantitatively. Comparative data is not included in this article.

ABSTRACT

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in the city of Wuhan, Hubei Province, China, in late 2019. Since then, the virus has spread globally and caused a pandemic. Assays that can measure the antiviral activity of antibodies or antiviral compounds are needed for SARS-CoV-2 vaccine and drug development. Here, we describe in detail a microneutralization assay, which can be used to assess in a quantitative manner if antibodies or drugs can block entry and/or replication of SARS-CoV-2 in vitro. 2020 Wiley Periodicals LLC. Basic Protocol 1: Microneutralization assay to test inhibition of virus by antibodies (purified antibodies or serum/plasma) Basic Protocol 2: Screening of anti-SARS-CoV-2 compounds in vitro Support Protocol: SARS-CoV-2 propagation.

FIGURES

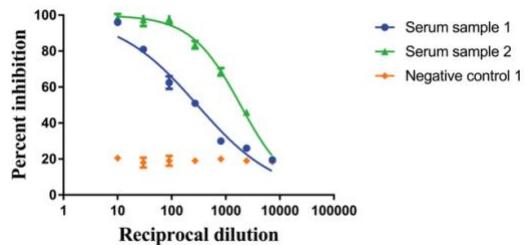


Figure 3 Analysis of data as reciprocal dilution of serum and percent inhibition of virus (ID50 of serum sample 1 is 1:298 and serum sample 2 is 1:1873).

MENTAL HEALTH & RESILIENCE NEEDS

COVID-19'S IMPACT ON HEALTHCARE WORKFORCE

EVALUATING THE EFFECTS OF THE COVID-19 PANDEMIC ON THE PHYSICAL AND MENTAL WELL-BEING OF OBSTETRICIANS AND GYNECOLOGISTS IN TURKEY

Yalçın Bahat P, Aldıkaçlıoğlu Talmaç M, Bestel A, Topbas Selcuki NF, Karadeniz O, Polat I.. Int J Gynaecol Obstet. 2020 Jun 30. doi: 10.1002/ijgo.13287. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

A survey of 253 obstetrician/gynecologists, administered by a group from the Department of Obstetrics and Gynecology at the Health Sciences University in Istanbul, Turkey between April 26th, 2020 and May 20th, 2020, found that 76.4% of respondents were anxious about contacting COVID-19 infected patients, 74.4% were afraid of getting sick, 59.8% felt their hospital's supply of PPE was adequate, and 72.4% had started to live separately from their families. These findings suggest that obstetrician/gynecologists have faced significant stressors during the COVID-19 pandemic. The authors also note that the results indicate that family support and finding coping mechanisms were important to respondents' management of stress related to the pandemic.

ABSTRACT

OBJECTIVE: To apply online surveying to assess the general physical and mental well-being of obstetricians/gynecologists (OB/GYNs) working in COVID-19 designated hospitals in Turkey. **METHODS:** A prospective survey-based study using an online survey platform. Three hundred participants working at COVID-19 designated hospitals in Turkey identified from a hospital database were sent a link to the survey by email between April 29 and May 20, 2020. **RESULTS:** A total of 253 OB/GYNs (31 consultants and 222 residents) completed the survey, for a response rate of 84.3%. Of respondents, 191 (76.4%) were anxious about coming into contact with pregnant women infected with COVID-19. 74.4% stated that they were afraid of getting sick. 64.8% reported that they had fallen into despair at times because of the pandemic. 66.5% stated that their family lives were affected. 72.4% started living separately from their families because of the pandemic. **CONCLUSION:** Despite the difficulties in patient care during the pandemic, OB/GYNs continued providing for their patients, which reflected positively on their perceptions of the profession. The importance of trust in the national healthcare system, presence of adequate PPE, finding a suitable coping mechanism, and family support were essential for Turkish OB/GYNs during the COVID-19 pandemic.

PSYCHIATRIC TRAINING DURING A GLOBAL PANDEMIC: HOW COVID-19 HAS AFFECTED CLINICAL CARE, TEACHING, AND TRAINEE WELL-BEING

Richards M, DeBonis K.. Psychiatr Serv. 2020 Jun 30:appips202000277. doi: 10.1176/appi.ps.202000277. Online ahead of print.

Level of Evidence: Other - Expert Opinion

BLUF

In this article, training directors of the psychiatry residency and fellowship program at UCLA outline the challenges they face in meeting the various needs of trainees during the ongoing pandemic. They advocate for consolidating and providing accurate COVID-19 related information to trainees, adopting telepsychiatry and remote teaching to reduce risk of infection to trainees and patients, and addressing trainees' basic and higher-level needs.

ABSTRACT

The COVID-19 pandemic has altered many aspects of personal and professional life, including how psychiatry is practiced and how trainees are taught. This Open Forum outlines the challenges faced by psychiatric training directors in adult as well as child and adolescent psychiatry in meeting the educational needs of trainees amid this international crisis. Prioritizing trainee protection and education as well as high-quality treatment for patients, the authors discuss effective communication strategies, rapid telepsychiatry expansion into clinical practice, curricular adjustments, and the importance of well-being. This Open Forum concludes with reflections and considerations for training directors as they prepare for subsequent stages of the COVID-19 pandemic.

IMPACT ON PUBLIC MENTAL HEALTH

AIR POLLUTION AND GERIATRIC MENTAL HEALTH: PERSPECTIVES ON THE COVID-19 PANDEMIC

Sharma R, Hossain MM, Pawar P, Sharma S.. Int Psychogeriatr. 2020 Jul 1:1-5. doi: 10.1017/S1041610220001428. Online ahead of print.

Level of Evidence: Other - Review / Literature Review

BLUF

In a literature review of household air pollution during the COVID-19 pandemic that assesses impacts of air quality on geriatric mental health, authors discuss recent air quality research, including work done by Liu et al (2020) which concluded solid fuel use (wood, dung, agricultural residues, coal, and charcoal) is associated with significantly higher Center for Epidemiologic Studies Depression Scale (CES-D) scores (0.59) and depression (odds ratio [OR]=1.26). Authors also report an association between fine particulate matter (diameter less than 2.5- μm) from woodsmoke and dementia rates for older adults, as indicated in a study by Oudin et al (2018). These findings suggest the need for increased ventilation and use of clean fuel to minimize incidence of adverse mental health outcomes in geriatric populations, and authors advocate for environmental factors (air quality, fuel usage) to be incorporated in psychogeriatric evidence of COVID-19 research as people are spending more time in their homes.

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