The Daily COVID-19 Literature Surveillance Summary

October 02, 2020

DISCLAIMER

This free and open source document represents a good faith effort to provide real time, distilled information for guiding best practices during the COVID-19 pandemic. This document is not intended to and cannot replace the original source documents and clinical decision making. These sources are explicitly cited for purposes of reference but do not imply endorsement, approval or validation.

This is not an official product or endorsement from the institutions affiliated with the authors, nor do the ideas and opinions described within this document represent the authors' or their affiliated institutions' values, opinions, ideas or beliefs. This is a good faith effort to share and disseminate accurate summaries of the current literature.

NOW LIVE!

Daily audio summaries of the literature in 10 minutes or less.
https://www.covid19lst.org/podcast/

COVID-19 Daily Literature Surveillance

COVID19LST

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

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table

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

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

EXECUTIVE SUMMARY

Epidemiology

- An analysis of 235 COVID-19 patients found a statistically significant association between sufficient Vitamin D levels (≥ 30ng/mL) and reduced disease severity, reduced hypoxia, reduced in-hospital mortality, increased lymphocyte percentage, and reduced CRP. Vitamin D sufficiency may reduce cytokine storm and overall immune response, clinically implicating Vitamin D sufficiency as a potentially key factor in reduced COVID-19 associated morbidity and mortality.

Understanding the Pathology

- A case study describes a 16-year-old male with COVID-19 who displayed cutaneous pityriasis rosea involving the trunk, oral hard and soft palates and was found to have positive serology titers for Epstein Barr virus (EBV), human herpes virus-7 (HHV-7), and human herpes virus-6 (HHV-6), with high avidity IgG against EBV and HHV-6, illustrating reactivation of latent infections. This suggests that SARS-CoV-2 infection and/or its inflammatory sequela may trigger reactivation of multiple latent infections, possibly contributing to the cutaneous manifestation in this case and the severe course of COVID-19 overall.

Transmission & Prevention

- Contract tracing data collected by the CDC from two counties in North Carolina found that 48% of COVID-19-positive individuals in Mecklenburg county and 35% in Randolph county reported no contacts, and from contacts that were named, 25% in Mecklenburg and 48% in Randolph could not be reached by phone after several attempts, suggesting the need for improved population engagement as well as punctuality in contact tracing to help control the spread of COVID-19 in the community.

Adjusting Practice During COVID-19

- Researchers in the United Kingdom and Sweden assessed the potential of SARS-CoV-2 droplet transmission (≤5 microns) via pulmonary function tests (PFTs) from healthy volunteers (n=33) and found that the highest amount of particles came from uncoordinated involuntary coughing, while relatively minute amounts came from coordinated voluntary breathing, suggesting that adaptation to PFT maneuvers to decrease time of breath holding and avoiding full expiration to reduce cough reflex would reduce droplet release.

- A 10-day randomized study of 208 individuals to evaluate the impact of performing activities that satisfy basic psychological needs (i.e. autonomy, competence, relatedness) during the COVID-19 outbreak found that individuals within the "basic psychological need-satisfying activities" intervention had increased need satisfaction and overall well-being and decreased perceived frustration and stress as compared to the control group.

TABLE OF CONTENTS

DISCLAIMER **2**

NOW LIVE! 2

LEVEL OF EVIDENCE **3**

EXECUTIVE SUMMARY **4**

TABLE OF CONTENTS **5**

CLIMATE **6**

Acceptability of a COVID-19 vaccine among adults in the United States: How many people would get vaccinated? 6

EPIDEMIOLOGY **8**

SYMPTOMS AND CLINICAL PRESENTATION 8

Adults *8*

Vitamin D sufficiency, a serum 25-hydroxyvitamin D at least 30 ng/mL reduced risk for adverse clinical outcomes in patients with COVID-19 infection 8

Unfolding of sickle cell trait by coronavirus disease 2019 (COVID-19) infection 10

UNDERSTANDING THE PATHOLOGY **11**

Human herpesvirus 6, 7 and Epstein Barr virus reactivation in pityriasis rosea during COVID-19 11

TRANSMISSION & PREVENTION **12**

COVID-19 Contact Tracing in Two Counties - North Carolina, June-July 2020 12

DEVELOPMENTS IN TRANSMISSION & PREVENTION 13

Inactivation of SARS-CoV-2 and HCoV-229E in vitro by ColdZyme® a medical device mouth spray against common cold 13

ADJUSTING PRACTICE DURING COVID-19 ..... **14**

MEDICAL SUBSPECIALTIES 14

Small Droplet Emission in Exhaled Breath During Different Breathing Manoeuvres: Implications for Clinical Lung Function Testing during COVID-19 14

Nephrology *14*

Nephrology and COVID-19 14

PSYCHIATRY 15

Basic Psychological Need-Satisfying Activities during the COVID-19 Outbreak 15

R&D: DIAGNOSIS & TREATMENTS **18**

DEVELOPMENTS IN DIAGNOSTICS 18

Highlighted prospects of an IgM/IgG antibodies test in identifying individuals with asymptomatic SARS CoV-2 infection 18

How Nanophotonic Label-Free Biosensors Can Contribute to Rapid and Massive Diagnostics of Respiratory Virus Infections: COVID-19 Case 19

ACKNOWLEDGEMENTS **21**

ACCEPTABILITY OF A COVID-19 VACCINE AMONG ADULTS IN THE UNITED STATES: HOW MANY PEOPLE WOULD GET VACCINATED?

Reiter PL, Pennell ML, Katz ML.. Vaccine. 2020 Sep 29;38(42):6500-6507. doi: 10.1016/j.vaccine.2020.08.043. Epub 2020 Aug 20.

Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

A cross-sectional survey study conducted by the College of Public Health and Comprehensive Cancer Center at Ohio State University in May 2020 among adults age 18 or older (n=2006) found that 69% (1374/2006) of participants were willing and 31% (632/2006) were not willing to get a COVID-19 vaccine, influenced by factors outlined in Table 3 and Figure 1. These findings suggest that there is a majority willingness to receive a COVID-19 vaccination, while also highlighting an opportunity to make educated efforts towards increasing vaccine acceptability among the general public.

ABSTRACT

BACKGROUND: Coronavirus disease 2019 (COVID-19) was declared a pandemic in March 2020. Several prophylactic vaccines against COVID-19 are currently in development, yet little is known about people's acceptability of a COVID-19 vaccine. METHODS: We conducted an online survey of adults ages 18 and older in the United States (n = 2,006) in May 2020. Multivariable relative risk regression identified correlates of participants' willingness to get a COVID-19 vaccine (i.e., vaccine acceptability). RESULTS: Overall, 69% of participants were willing to get a COVID-19 vaccine. Participants were more likely to be willing to get vaccinated if they thought their healthcare provider would recommend vaccination (RR = 1.73, 95% CI: 1.49-2.02) or if they were moderate (RR = 1.09, 95% CI: 1.02-1.16) or liberal (RR = 1.14, 95% CI: 1.07-1.22) in their political leaning. Participants were also more likely to be willing to get vaccinated if they reported higher levels of perceived likelihood getting a COVID-19 infection in the future (RR = 1.05, 95% CI: 1.01-1.09), perceived severity of COVID-19 infection (RR = 1.08, 95% CI: 1.04-1.11), or perceived effectiveness of a COVID-19 vaccine (RR = 1.46, 95% CI: 1.40-1.52). Participants were less likely to be willing to get vaccinated if they were non-Latinx black (RR = 0.81, 95% CI: 0.74-0.90) or reported a higher level of perceived potential vaccine harms (RR = 0.95, 95% CI: 0.92-0.98). CONCLUSIONS: Many adults are willing to get a COVID-19 vaccine, though acceptability should be monitored as vaccine development continues. Our findings can help guide future efforts to increase COVID-19 vaccine acceptability (and uptake if a vaccine becomes available).

FIGURES

Table 3
Bivariate correlates of COVID-19 vaccine acceptability for continuous variables.

	Mean (SD)		
	Not Willing (n = 632)	Willing (n = 1374)	Bivariate RR (95% CI)
Knowledge about COVID-19 infection[a]	0.71 (0.23)	0.76 (0.18)	1.54 (1.31–1.82)**
Perceived likelihood of COVID-19 infection in the future[b]	2.20 (0.78)	2.53 (0.73)	1.19 (1.15–1.24)**
Perceived severity of COVID-19 infection[c]	2.72 (1.04)	3.22 (0.82)	1.21 (1.17–1.26)**
Perceived stigma of COVID-19 infection[d]	2.47 (0.92)	2.44 (0.97)	0.99 (0.96–1.02)
Perceived effectiveness of a COVID-19 vaccine[e]	2.24 (0.86)	3.25 (0.66)	1.62 (1.56–1.68)**
Perceived potential harms of a COVID-19 vaccine[f]	3.87 (0.97)	3.73 (0.83)	0.94 (0.91–0.98)*
Perceived unavailability of a COVID-19 vaccine[f]	2.61 (1.05)	2.65 (1.25)	1.01 (0.99–1.03)
Self-efficacy to engage in protective behaviors against COVID-19[f]	4.24 (0.87)	4.39 (0.75)	1.08 (1.03–1.13)**
Perceived positive social norms of protective behaviors against COVID-19 in community[f]	3.67 (1.05)	3.93 (1.01)	1.08 (1.05–1.12)**

Note. COVID-19 = coronavirus disease 2019; RR = relative risk; CI = confidence interval.
[a] Proportion of five knowledge items answered correctly (possible range = 0–1).
[b] 1 item; 4-point response scale ranging from "no chance" to "high chance" (possible range = 1–4).
[c] 1 item; 4-point response scale ranging from "not at all" to "very" (possible range = 1–4).
[d] 4 item scale; each item had a 5-point response scale ranging from "strongly disagree" to "strongly agree" (possible range = 1–5).
[e] 1 item; 4-point response scale ranging from "not at all" to "a lot" (possible range = 1–4).
[f] 1 item; 5-point response scale ranging from "strongly disagree" to "strongly agree" (possible range = 1–5).
* $p < 0.05$;
** $p < 0.001$; † $p < 0.20$;

Table 3: Bivariate correlates of COVID-19 vaccine acceptability for continuous variables.

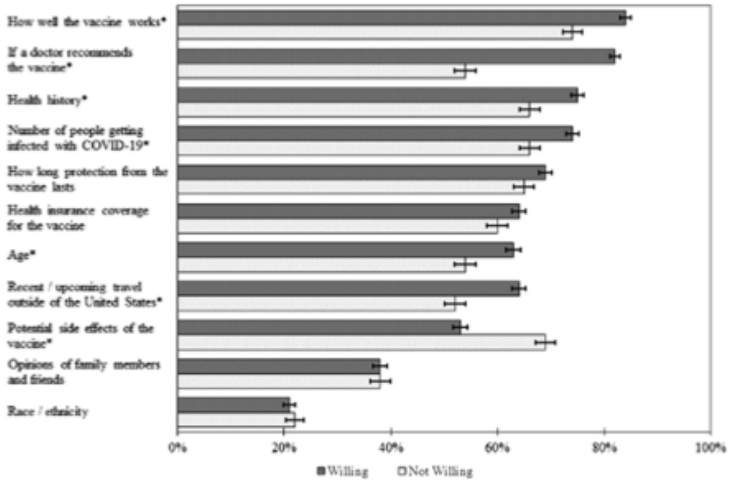

Fig. 1. Factors that would matter in participants' decisions about COVID-19 vaccination by vaccine willingness. Bars indicate standard errors. '*' indicates a comparison with $p < 0.05$, based on chi-square tests with the Bonferroni adjustment to account for multiple testing.

ADULTS

VITAMIN D SUFFICIENCY, A SERUM 25-HYDROXYVITAMIN D AT LEAST 30 NG/ML REDUCED RISK FOR ADVERSE CLINICAL OUTCOMES IN PATIENTS WITH COVID-19 INFECTION

Maghbooli Z, Sahraian MA, Ebrahimi M, Pazoki M, Kafan S, Tabriz HM, Hadadi A, Montazeri M, Nasiri M, Shirvani A, Holick MF.. PLoS One. 2020 Sep 25;15(9):e0239799. doi: 10.1371/journal.pone.0239799. eCollection 2020.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

A cross-sectional analysis of 235 COVID-19 patients in Sina Hospital, Tehran, Iran through May 1, 2020 found a statistically significant association between sufficient Vitamin D levels (≥ 30ng/mL) and reduced disease severity, reduced hypoxia, reduced in-hospital mortality, increased lymphocyte percentage, and reduced CRP. The physicians hypothesize that Vitamin D sufficiency may reduce cytokine storm and overall immune response (Tables 3 & 4), clinically implicating Vitamin D sufficiency as a potentially key factor in reduced COVID-19 associated morbidity and mortality (Figure 1).

SUMMARY

Serum levels of 25-hydroxycholecalciferol (25(OH)D) more than or equal to 30ng/ml is considered sufficient. The authors observed the following findings:
- 32.8% of patients had sufficient Vitamin D levels.
- 74% of patients had severe COVID-19 infection based on CDC criteria.
- A statistically significant association was found between Vitamin D levels and disease severity (p=0.02), hypoxic risk (p=0.004), unconsciousness (p=0.03), in-hospital mortality (p=0.04), and lymphocyte percentage (p=0.03), and quantitative CRP (p=0.01) were observed (Tables 3 & 4).
- None of the patients younger than 40 years died from COVID-19.
- 206 patients were older than 40 years old. Among them, 20% had Vitamin D levels <30ng/ml and only 9.7% had Vitamin D levels of at least 30ng/ml (p=0.04).
- 16.3% of patients 40 years and older succumbed to COVID-19, while only 6.3% older than 40 years died with 25(OH)D ≥ 40ng/ml (Figure 1).

ABSTRACT

BACKGROUND: To investigate the association between serum 25-hydroxyvitamin D levels and its effect on adverse clinical outcomes, and parameters of immune function and mortality due to a SARS-CoV-2 infection. STUDY DESIGN: The hospital data of 235 patients infected with COVID-19 were analyzed. RESULTS: Based on CDC criteria, among our study patients, 74% had severe COVID-19 infection and 32.8% were vitamin D sufficient. After adjusting for confounding factors, there was a significant association between vitamin D sufficiency and reduction in clinical severity, inpatient mortality serum levels of C-reactive protein (CRP) and an increase in lymphocyte percentage. Only 9.7% of patients older than 40 years who were vitamin D sufficient succumbed to the infection compared to 20% who had a circulating level of 25(OH)D< 30 ng/ml. The significant reduction in serum CRP, an inflammatory marker, along with increased lymphocytes percentage suggest that vitamin D sufficiency also may help modulate the immune response possibly by reducing risk for cytokine storm in response to this viral infection. CONCLUSION: Therefore, it is recommended that improving vitamin D status in the general population and in particular hospitalized patients has a potential benefit in reducing the severity of morbidities and mortality associated with acquiring COVID-19.

Clinical outcomes	25OHD ≥30 N = 77	25OHD < 30 N = 158	P-value
Hospitalization (day)†	5 (5)	5 (5)	0.28
Duration from illness onset to first admission (day) †	7 (7)	7 (7)	0.30
Chest pain ‡	14.3% (11)	8.2% (13)	0.17
Dyspnea ‡	51.9% (40)	60.1% (95)	0.26
ICU admission ‡	14.3% (11)	20.9% (33)	0.33
Acute respiratory distress syndrome ‡	11.7% (9)	17.1% (27)	0.33
Intubation ‡	7.8% (6)	11.4% (18)	0.49
Multi-organ damage ‡	13% (10)	17.7% (28)	0.45
Acute kidney injury ‡	13% (10)	15.2% (24)	0.69
Bilateral lung involvement‡	31.7 (19)	33.3% (43)	0.86
Shock‡	6.5 (5)	10.8% (17)	0.34
Unconsciousness	1.3%(1)	8.2%(13)	0.03
Hypoxia† b	19.4% (15)	39.2%(62)	0.004
Quantitative C-reactive protein (CRP)>40mg/L ‡	61(47)	77.2(122)	0.01
blood lymphocyte percentage<20% ‡	45.5(35)	60.1(95)	0.03
Severity † c	63.6% (49)	77.2%(122)	0.02

Numerical variables were expressed as median (IQR). Categorical variables were presented as percentages.
Hospitalization range: 1–23 days in patients with vitamin D deficiency/insufficiency and 1–19 days in patients with vitamin D sufficiency.
Duration form illness onset to first admission: 0–30 days in patients with vitamin D deficiency/insufficiency and 0–21 days in patients with vitamin D sufficiency.
† median (IQR),
‡ % (N),
[a] only in patients older than 40 years,
[b] defined as an arterial blood oxygen saturation levels below 90%,
[c] Severe-critical.

Table 3: The COVID-19 clinical outcomes based on vitamin D status.

Clinical outcomes	Relative Risk	95% CI (lower, upper)	P-value
Severity ‡	1.59	1.05, 2.41	**0.02**
Unconsciousness	1.07	1.02, 1.13	**0.03**
Hypoxia† b	1.32	1.11, 1.57	**0.004**
C-reactive protein (CRP)>40mg/L	1.7	1.13,2.56	**0.01**
lymphocyte percentage<20%	1.36	1.03, 1.80	**0.03**

Values in bold indicate statistical significance (P<0.05).
† Only in patients older than 40 years.
‡ Severe-critical.

Table 4: Relative risk of COVID-19 clinical outcomes associated with patients who had a 25(OH)D<30 ng/mL.

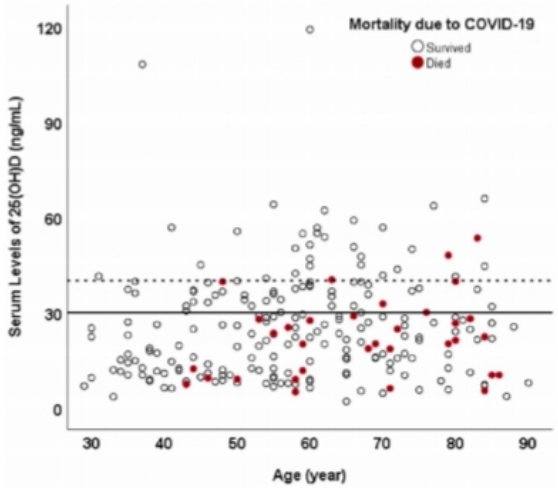

Figure 1: The association between vitamin D status and inpatient mortality because of COVID-19. A scatter plot relating mortality in patients with a serum 25(OH)D level. The red dots represent the inpatients who perished and the black dots represented the patients who have survived. The solid black line separates the patients with vitamin D deficiency/ insufficiency (below the solid line) from the vitamin D sufficient patients (above the solid line). The number of red dots (inpatient mortality) above the solid line is significantly less compared to the dots below the line. Also, the trend of reducing inpatient mortality is continued for higher levels of serum 25(OH)D. The dotted line represents a serum level of 25(OH)D of 40 ng/mL. The mortality (red dots) is very rare in patients with serum 25(OH)D of at least 40ng/mL (above the dotted line). An evaluation of mortality in the patient population revealed that no one under the age of 40 years died as a result of being infected with COVID 19. However 16.3% of patients 40 years and older succumbed to the infection. Of the 206 patients who were 40 years and older, 20% had a blood level of 25(OH)D<30 ng/mL whereas only 9.7% who perished had a blood level of 25OH)D of at least 30 ng/mL(p = 0.04). Furthermore only 6.3% of the patients over 40 years of age died with a blood level of 25(OH)D of 40 ng/mL or higher.

UNFOLDING OF SICKLE CELL TRAIT BY CORONAVIRUS DISEASE 2019 (COVID-19) INFECTION

Sheha D, El-Shayeb M, Eid Y, Amin M, Saeed A, Abdou D, Aly T, Samy S, Elziaty R, Aboelyazed S, Osman A, Sheha A.. Br J Haematol. 2020 Sep 23. doi: 10.1111/bjh.17089. Online ahead of print.
Level of Evidence: 5 - Case report

BLUF

This case report by internists and radiologists at Ain Shams University in Cairo, Egypt describes a 22-year-old female with a history of splenectomy and chronic recurring bony aches who presented initially with fever, bony aches, tachycardia, and tachypnea. She ultimately tested positive for SARS-CoV-2 and was admitted for COVID-19 pneumonia complicated by autoimmune hemolytic anemia and thrombocytopenia. On follow-up, computed tomography showed osteonecrosis and "fish-shaped" vertebrae suggesting sickle cell disease (SCD; Figures 1,2) and sickle cell trait was confirmed via electrophoresis. Authors suggest that patients with SCD may be at higher risk for a severe COVID-19 course.

FIGURES

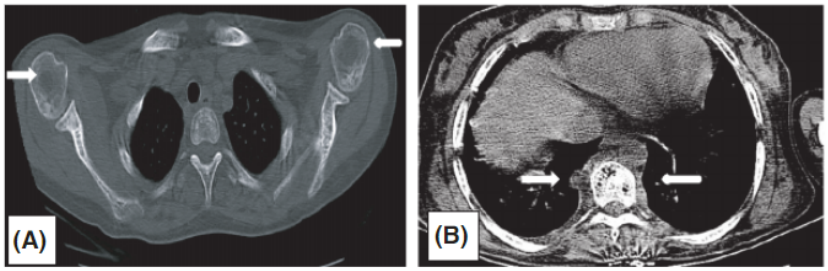

Figure 1. High-resolution computed tomography (HRCT) of the chest. (A) Bone window of chest CT showing exaggerated marrow trabeculae of both scapulae and ribs. Both humeral heads show lytic lesions suggestive ofosteonecrosis. (B) Mediastinal window of CT chest showing paraspinal soft tissue mass bilaterally in the thoracic region, denoting extramedullary haemopoiesis.

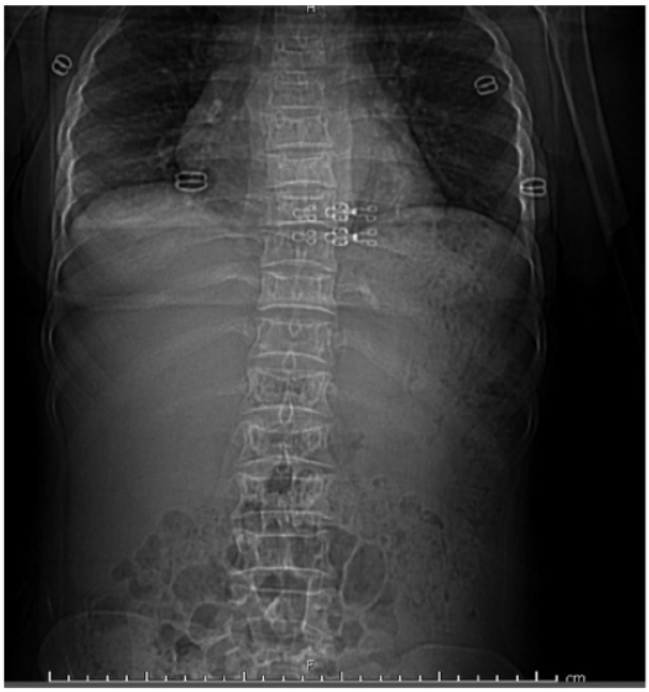

Figure 2. Scout image for chest computed tomography showing bilateral paraspinal shadows due to extra-medullary haemopoiesis. Vertebral bodies in the thoracic and lumbar region are 'H'-shaped with exaggerated marrow trabeculae, suggestive of sickle cell disease.

HUMAN HERPESVIRUS 6, 7 AND EPSTEIN BARR VIRUS REACTIVATION IN PITYRIASIS ROSEA DURING COVID-19

Drago F, Ciccarese G, Rebora A, Parodi A.. J Med Virol. 2020 Sep 24. doi: 10.1002/jmv.26549. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

Researchers from the Dermatology department at Ospedale Policlinico San Martino and University of Genoa, Italy describe a 16-year-old male with COVID-19 who displayed cutaneous pityriasis rosea (PR) involving the trunk and oral hard and soft palates (Figure 1). Further investigation revealed positive serology titers for Epstein Barr virus (EBV), human herpes virus-7 (HHV-7), and human herpes virus-6 (HHV-6). Additionally, viral DNA for EBV and HHV-6 was detected along with high avidity IgG against these two viruses, illustrating reactivation of latent infections. The authors suggest that SARS-CoV-2 infection and/or its inflammatory sequela may trigger reactivation of multiple latent infections, possibly contributing to the cutaneous manifestation in this case and the severe course of COVID-19 overall.

ABSTRACT

Cutaneous manifestations during Coronavirus Disease 2019 (COVID-19) include pityriasis rosea (PR) and PR-like eruptions1-3 . We describe a patient with PR demonstrating that concurrent viral reactivations may occur during COVID-19.

FIGURES

Figure 1. Erythematous macules and petechiae on the hard and soft palate

COVID-19 CONTACT TRACING IN TWO COUNTIES - NORTH CAROLINA, JUNE-JULY 2020

Lash RR, Donovan CV, Fleischauer AT, Moore ZS, Harris G, Hayes S, Sullivan M, Wilburn A, Ong J, Wright D, Washington R, Pulliam A, Byers B, McLaughlin HP, Dirlikov E, Rose DA, Walke HT, Honein MA; Contact Tracing Assessment Team, Moonan PK, Oeltmann JE.. MMWR Morb Mortal Wkly Rep. 2020 Sep 25;69(38):1360-1363. doi: 10.15585/mmwr.mm6938e3.
Level of Evidence: 3 - Local non-random sample

BLUF

The Contact Tracing Assessment Team at the CDC report contract tracing data collected between June 1st to June 30th, 2020 in Mecklenburg county and between June 15th to July 12th, 2020 in Randolph county, North Carolina. They found that 48% of COVID-19-positive individuals in Mecklenburg and 35% in Randolph reported no contacts. Additionally, from contacts that were named, 25% in Mecklenburg and 48% in Randolph could not be reached by phone after several attempts (Table). Based on these observations, the authors urge for improved population engagement as well as punctuality in contact tracing to help control the spread of COVID-19 in the community.

ABSTRACT

Contact tracing is a strategy implemented to minimize the spread of communicable diseases (1,2). Prompt contact tracing, testing, and self-quarantine can reduce the transmission of SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19) (3,4). Community engagement is important to encourage participation in and cooperation with SARS-CoV-2 contact tracing (5). Substantial investments have been made to scale up contact tracing for COVID-19 in the United States. During June 1-July 12, 2020, the incidence of COVID-19 cases in North Carolina increased 183%, from seven to 19 per 100,000 persons per day* (6). To assess local COVID-19 contact tracing implementation, data from two counties in North Carolina were analyzed during a period of high incidence. Health department staff members investigated 5,514 (77%) persons with COVID-19 in Mecklenburg County and 584 (99%) in Randolph Counties. No contacts were reported for 48% of cases in Mecklenburg and for 35% in Randolph. Among contacts provided, 25% in Mecklenburg and 48% in Randolph could not be reached by telephone and were classified as nonresponsive after at least one attempt on 3 consecutive days of failed attempts. The median interval from specimen collection from the index patient to notification of identified contacts was 6 days in both counties. Despite aggressive efforts by health department staff members to perform case investigations and contact tracing, many persons with COVID-19 did not report contacts, and many contacts were not reached. These findings indicate that improved timeliness of contact tracing, community engagement, and increased use of community-wide mitigation are needed to interrupt SARS-CoV-2 transmission.

FIGURES

Metrics	Mecklenburg County*	Randolph County*
No. of specimens tested	61,979	6,292
Case investigation, no. (%)		
Positive laboratory reports received†	8,097 (13)	707 (11)
Laboratory-confirmed COVID-19 cases	7,116 (88)§	589 (83)§
Laboratory-confirmed COVID-19 cases lost to follow-up	1,602 (23)¶	5 (1)**
Laboratory-confirmed COVID-19 cases with initial investigation	5,514 (77)	584 (99)
Laboratory-confirmed COVID-19 cases with initial investigation with no contacts named	2,624 (48)	202 (35)
Laboratory-confirmed COVID-19 cases with named contacts	2,890 (52)	382 (66)
Contact tracing, no. (%)		
No. of Identified contacts	13,401††	1,146
Identified contacts lost to follow-up	3,331 (25)¶	544 (47)¶
Identified contacts opted out of health department daily monitoring	255 (2)	50 (4)
Identified contacts who agreed to self-quarantine and 14-day monitoring	9,815 (73)§§	552 (48)§§
Identified contacts who agreed to self-quarantine and subsequently had a positive test result	137¶¶	69***
Time intervals, no. of days (range)		
From specimen collection to reported results	2 (0–29)	3 (0–15)
From specimen collection to case investigation	4 (0–38)	3 (0–36)
From case investigation to contact notification	1 (0–25)	3 (0–26)
From specimen collection to contact notification and presumed start of quarantine	6 (1–38)	6 (0–58)

Abbreviation: COVID-19 = coronavirus disease 2019.
* In some cases, column percentages within a category might not sum to 100% because of rounding.
† Difference between positive laboratory reports received and laboratory-confirmed cases (981 in Mecklenburg County and 118 in Randolph County) reflects testing of residents from other jurisdictions or repeat testing.
§ Cases in county residents; the remaining cases were in residents of other jurisdictions or retests.
¶ Could not be reached via phone after 3 consecutive days of failed attempts, or if contact information was missing or invalid.
** Could not be reached via phone after 3 consecutive days of failed attempts and a visit by local law enforcement to the residential address provided, or if contact information was missing or invalid.
†† Does not include contacts identified during investigations of congregate settings or large workplace investigations.
§§ Contacts were monitored by the health department.
¶¶ The total number of contacts who volunteered to be tested is unknown.
*** In total, 293 contacts volunteered to be tested.

TABLE. COVID-19 contact tracing metrics in two counties — North Carolina, June–July 2020

INACTIVATION OF SARS-COV-2 AND HCOV-229E IN VITRO BY COLDZYME® A MEDICAL DEVICE MOUTH SPRAY AGAINST COMMON COLD

Gudmundsdottir Á, Scheving R, Lindberg F, Stefansson B.. J Med Virol. 2020 Sep 25. doi: 10.1002/jmv.26554. Online ahead of print.

Level of Evidence: 5 - Mechanism-based reasoning

BLUF

An in vitro study conducted by several academic professors at the University of Iceland (who are each at least partially employed by Enzymatica, the maker of ColdZyme) examined the effectiveness at which ColdZyme (CZ-MD), a commercially available mouth spray device for common cold prevention, could deactivate SARS-CoV-2 and HCoV-229E (one coronavirus causing the common cold) in vitro. Results of a viral suspension test revealed that CZ-MD achieved 98.3% inactivation of SARS-CoV-2 and 99.9% inactivation of HCoV-229E (Table 1), suggesting a potential for CZ-MD to limit SARS-CoV-2 infection risk through the mouth. However, ColdZyme's effectiveness remains uncertain as in vivo CZ-MD concentrations may be insufficient to inactivate SARS-CoV-2, and the spray does no protect against nasal inhalation of the virus.

ABSTRACT

BACKGROUND: The COVID-19 pandemic calls for effective and safe treatments. SARS-CoV-2 causing COVID-19 actively replicates in the throat, unlike SARS-CoV, and shows high pharyngeal viral shedding even in patients with mild symptoms of the disease. HCoV-229E is one of four coronaviruses causing the common cold. In this study, the efficacy of ColdZyme (CZ-MD), a medical device mouth spray, was tested against SARS-CoV-2 and HCoV-229E in vitro. The CZ-MD provides a protective glycerol barrier containing cod trypsin as an ancillary component. Combined, these ingredients can inactivate common cold viruses in the throat and mouth. The CZ-MD is believed to act on the viral surface proteins that would perturb their entry pathway into cells. The efficacy and safety of the CZ-MD has been demonstrated in clinical trials on the common cold. METHOD OF STUDY: The ability of the CZ-MD to inactivate SARS-CoV-2 and HCoV-229E was tested using an in vitro virucidal suspension test (ASTM E1052). RESULTS: CZ-MD inactivated SARS-CoV-2 by 98.3% and HCoV-229E by 99.9%. CONCLUSION: CZ-MD mouth spray can inactivate the respiratory coronaviruses SARS-CoV-2 and HCoV-229E in vitro. Although the in vitro results presented cannot be directly translated into clinical efficacy, the study indicates that CZ-MD might offer a protective barrier against SARS-CoV-2 and a decreased risk of COVID-19 transmission. This article is protected by copyright. All rights reserved.

FIGURES

Virus	Sample	Input Load $log_{10}TCID50$ (Mean)†	Output Load $log_{10}TCID50$ (Mean± SD)	log_{10} Reduction (Mean)	Percent Inactivation
SARS-CoV-2, strain USA-WA1/2020, BEI Resources NR-52281	CZ-MD	6.06	4.30±0.21	1.76	98.3
	Reference agent (2000 ppm NaOCl)		≤ 1.61	≥ 4.45	
Human Coronavirus (HCoV), strain 229E, ATCC VR-740	CZ-MD	5.55	2.67±0.13	2.88	99.9
	Reference agent (2000 ppm NaOCl)		≤ 1.31	≥ 4.24	

†Mean of two experimental values

Table I. Inactivation of SARS-CoV-2 and HCoV-229E by ColdZyme® (CZ-MD)

ADJUSTING PRACTICE DURING COVID-19

MEDICAL SUBSPECIALTIES

SMALL DROPLET EMISSION IN EXHALED BREATH DURING DIFFERENT BREATHING MANOEUVRES: IMPLICATIONS FOR CLINICAL LUNG FUNCTION TESTING DURING COVID-19

Greening NJ, Larsson P, Ljungström E, Siddiqui S, Olin AC.. Allergy. 2020 Sep 23. doi: 10.1111/all.14596. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Researchers affiliated with respiratory sciences and public health from the United Kingdom and Sweden assessed the potential of SARS-CoV-2 droplet transmission (≤5 microns) via pulmonary function tests (PFTs) from healthy volunteers (n=33) and found the highest amount of particles came from uncoordinated involuntary coughing while relatively minute amounts came from coordinated voluntary breathing (Figure 1). Given that PFTs are essential for diagnosis and treatment of many pulmonary conditions, authors suggest not deferring these tests during the COVID-19 pandemic but rather adapting to reduce droplet release by decreasing time of breath holding and avoiding full expiration to reduce cough reflex.

FIGURES

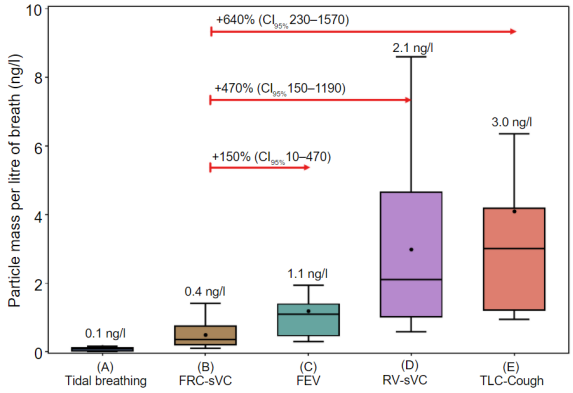

Figure 1. Mass of exhaled particles per breath using PExA following different breathing maneuvers. Median values are shown above each plot. Box and whisker plots are median (line), mean (dot) with interquartile range (box) and range (whiskers). (A) Tidal Volume (B) slow Vital Capacity following inspiration from Functional Residual Capacity (C) Forced Expiratory Volume (D) slow Vital Capacity from Residual Volume (E) Cough from Total Lung Capacity

NEPHROLOGY

NEPHROLOGY AND COVID-19

Winkelmayer WC, Khairallah P, Charytan DM.. JAMA. 2020 Sep 22;324(12):1137-1138. doi: 10.1001/jama.2020.16779.
Level of Evidence: Other - Expert Opinion

BLUF

In this viewpoint article, nephrologists from Baylor College of Medicine and New York University Grossman School of Medicine report on emerging difficulties of nephrology care in the setting of COVID-19 including delayed kidney transplants, adjusting care to comply with social distancing regulations, and renal complications directly impacting those infected with SARS-CoV-2 (some cases leading to continuous kidney replacement therapy [CKRT] and dialysis). Despite these challenges, authors highlight adaptations to continue effective nephrology care such as using older technology and dialysis machines in low supply settings, outpatient dialysis COVID-19 screening and scheduling plans for reduced transmission risk, and telehealth implementation when appropriate.

BASIC PSYCHOLOGICAL NEED-SATISFYING ACTIVITIES DURING THE COVID-19 OUTBREAK

Behzadnia B, FatahModares S.. Appl Psychol Health Well Being. 2020 Sep 24. doi: 10.1111/aphw.12228. Online ahead of print.
Level of Evidence: 2 - Randomized trial or observational study with dramatic effect

BLUF

Researchers affiliated with the University of Tabriz and Urmia University in Iran performed a 10-day randomized research study (n=208) to evaluate the impact of performing activities that satisfy basic psychological needs (i.e. autonomy, competence, relatedness) during the COVID-19 outbreak (Figure 1). They found that individuals within the "basic psychological need-satisfying activities" intervention (n=98; Table 1) had increased need satisfaction and overall well-being ($p<0.001$) and decreased perceived frustration and stress ($p<0.001$) as compared to the control group (n=110; Figure 2). These findings suggest that engaging in activities fulfilling basic psychological needs may help people cope during the pandemic and improve well-being.

ABSTRACT

BACKGROUND: The rapidly spreading novel coronavirus outbreak (COVID-19) worldwide may increase fear and stress, and has a cost for people's well-being and their motivation toward activities. In this study, we applied principles from Self-Determination Theory to develop and test activities to satisfy basic psychological needs (autonomy, competence, and relatedness) to enhance the experience of need satisfaction, autonomous self-regulation, and subjective vitality, and to decrease the experience of need frustration, controlled self-regulation, amotivation, and perceived stress. METHOD: Using a 10-day experimental research design among an Iranian sample (N = 208, Mage = 23.52, SD = 5.00), we randomly allocated participants to either an experimental (basic psychological need-satisfying activities intervention, n = 98) or a control (neutral comparison group, n = 110) condition. RESULTS: Repeated measure ANCOVA showed that participants in the experimental condition reported greater psychological need satisfaction, autonomous self-regulation, subjective vitality, and lesser psychological need frustration, amotivation, and perceived stress than did participants in the control condition. CONCLUSION: We conclude that the intervention was successful in helping participants enhance their motives and well-being and reduce their stress when life is surrounded by uncertainty and during social distancing restrictions.

FIGURES

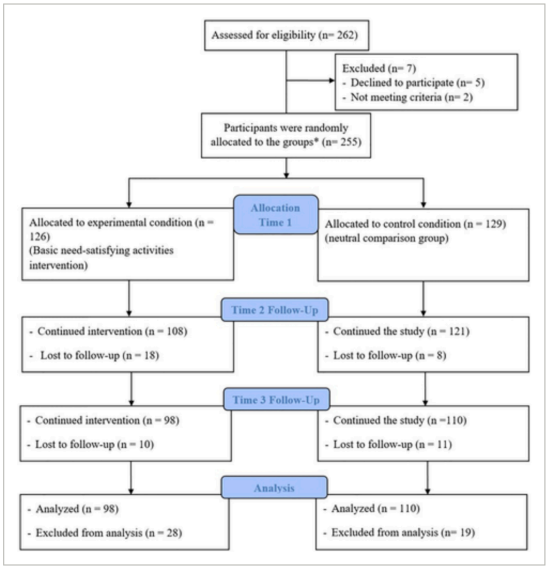

FIGURE 1

Open in figure viewer | ⬇F

Participants flowchart. * Teachers of the participants were randomly allocated to groups.

FIGURE 1. Participants flowchart. * Teachers of the participants were randomly allocated to groups.

Day	Intervention
Day 1 (Autonomy, competence, relatedness)	Today, try to do something that you have done before that has been a challenge for you, but something that you feel you can do it successfully (e.g. doing a specific exercise, or making a special dish or cake). To do this, first try to do it yourself, create the conditions for those around you (e.g. family members and your friends) to be able to do this, and then encourage and support them to do it
Day 2 (Autonomy, relatedness)	Today, try to do something that makes you feel that you can help someone (e.g. teaching someone an important task even if a simple thing). To do this, try to feel responsible for teaching it today, and encourage and support those around you (or even yourself), teach it to others, and try to create the conditions for your family members (or your friends) to make the effort and perform it
Day 3 (Relatedness)	Today, do something that makes you feel good in connection with nature, and take inspiration from it to do your daily activities (such as making a pot or flower at home, or arranging pots). To do this, try to make a good connection with nature, and encourage/support those around you (e.g. family members or friends) to do so; meanwhile, try to be less in touch with artificial things like television and your mobile
Day 4 (Autonomy, relatedness)	Today, try to use positive dialogue with others, so that you speak positively about your feelings and thoughts (e.g. using words like "How good it is that you are here", or appreciating others). To fulfill this, try to use only positive words in your daily interaction with others, and encourage/support those around you to do so; in the meantime, try not to think about negative events and dialogue, nor judge them
Day 5 (Autonomy, competence, relatedness)	Today, try to make a meaningful choice about what matters to you, even if it is a very small thing (e.g. the decision to attain a goal like a healthy lifestyle or learning a foreign language, or make a plan or a framework for your work). To do this, try both to make meaningful choices for yourself, and to encourage/support those around you. Try to create the conditions to fulfill it for those around you (e.g. family members and friends)
Day 6 (Competence)	Today, try to come up with creative work or ideas for the first time. Let yourself enjoy and be surprised with the result (e.g. making something or a device with your extras at home, or any other creative stuff). To fulfill this, both do it yourself and encourage/support those around you to do so. Try to create a condition for those around you (e.g. family members and friends) to perform it well
Day 7 (Autonomy, competence, relatedness)	Today, try to do a joyful exercise with family members. At the same time, smile during the exercise. Don't think about anything other than the exercise and just smiling and think about your breathing. Try to encourage/support those around you, regardless of whether they perform the exercise well or poorly. If you are alone at home, try to do this online by creating a group via social media applications, such as Skype or WhatsApp
Day 8 (Competence, relatedness)	Try to share an experience or an event with others that has directed your life, and made it meaningful. Share your compelling experiences with others so they may be useful and positive for them too
Day 9 (Autonomy, competence, relatedness)	Today, try to do your favorite personal activities, things that you would like to do, but remember to be active and transfer your positive energy to the people around you, and in the meantime try to focus on your daily activities (e.g. studying, jobs, doing exercises, or helping your family members)
Day 10 (Autonomy, competence, relatedness)	Today, try to write a paragraph (or how much you want) about your emotions, thoughts, and experiences during these 10 days and share it with ones you love or whomever you think that it can be useful to in such days. Always keep in your mind that: one of the greatest and most beautiful feelings in the world is to be compassionate and kind. There is always time to live well, so you can just start it and remind others to do it as well. Determine the best things in your life by yourself, and finally try to be the best within yourself

Table 1. Instructions for Basic Psychological Need-Satisfying Activities Intervention

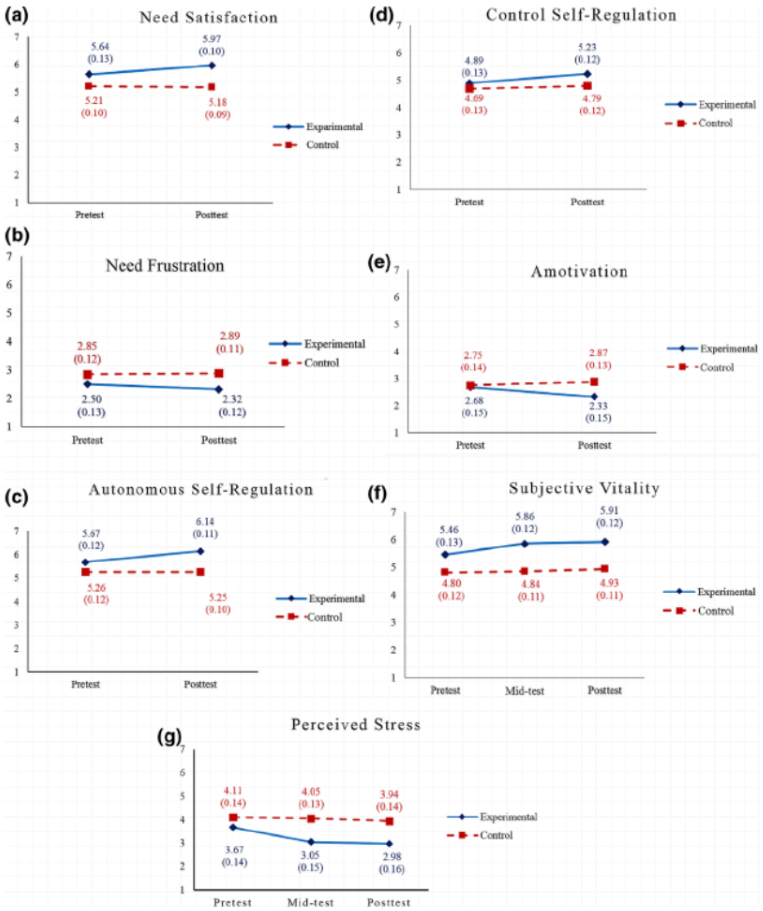

Figure 2. Participants' experience of basic needs (a, b), motivational self-regulation (c, d, e), subjective vitality (f), and perceived stress (g). Note. Numbers within parentheses are standard errors.

HIGHLIGHTED PROSPECTS OF AN IGM/IGG ANTIBODIES TEST IN IDENTIFYING INDIVIDUALS WITH ASYMPTOMATIC SARS COV-2 INFECTION

Li Y, He Q, Yu R, Jiang H, Wang W, Feng D, Hou G, Zhou H, Jiang Y, Xiang Z.. Arch Pathol Lab Med. 2020 Sep 23. doi: 10.5858/arpa.2020-0310-SA. Online ahead of print.
Level of Evidence: 4 - Case-control studies, or "poor or non-independent reference standard

BLUF

A retrospective cohort study conducted across various medical institutions in China involving 389 individuals having close contacts with COVID-19 found 89/389 tested positive for SARS-CoV-2 via nucleic acid test. Additionally, 225/300 who tested negative twice exhibited CT evidence of pneumonia. Of these 225 patients, 212 were found to be SARS-CoV-2 positive via IgM or IgG. These findings suggest a benefit to using IgM/IgG antibody detection in conjunction with nucleic acid tests and pulmonary CT scanning to identify asymptomatic SARS CoV-2 infection.

ABSTRACT

Context, Covert severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections could be seeding new outbreaks. How to identify asymptomatic SARS-CoV-2 infections early has become a global focus. Objective, To explore the roles of immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies detection, nucleic acid tests and computed tomography (CT) scanning to identify asymptomatic SARS-CoV-2 infection. Design, The clinical data of 389 individuals with close contacts including in general characteristics, SARS-CoV-2 etiology, serum-specific IgM and IgG antibody detection and CT imaging results, were systematically analyzed. Results, The present study showed that only 89 of the 389 individuals with close contacts were positive after the first nucleic acid test, while 300 individuals were still negative after two nucleic acid tests. Among the 300 individuals, 75 did not have pneumonia, and the other 225 individuals had pulmonary imaging changes. A total of 143 individuals were eventually diagnosed as having asymptomatic infection through IgM antibody and IgG antibody detection. The sensitivity, specificity and false-negative rate of IgM and IgG antibody detection were approximately 97.1% (347/357), 95.3% (204/214) and 4.67% (10/214), respectively. It also indicated that over approximately 2 weeks, most individuals were both IgM positive and IgG positive, accounting for 68.57% (72/105). Over approximately 3 weeks, the proportion of IgM-positive and IgG-positive individuals decreased to 8.57% (9/105), and the proportion of IgM-negative and IgG-positive individuals increased to 76.19% (80/105). Conclusions, There are highlighted prospects of IgM/IgG antibody detection as a preferred method in identifying the individuals with asymptomatic SARS CoV-2 infection, especially combined with nucleic acid tests and pulmonary CT scanning.

FIGURES

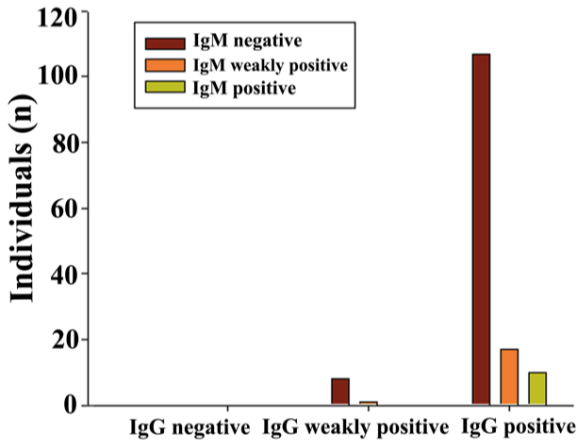

Figure 4. Definitive diagnosis of 143 asymptomatic individuals in whom two nucleic acid tests were negative confirmed using IgM and IgG antibodies detection. 143 asymptomatic SARS CoV-2 infections who were nucleic acid test negative were confirmed using IgM and IgG antibodies detection.

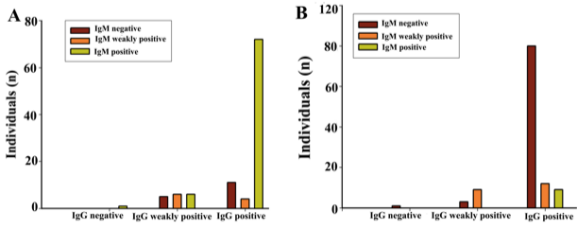

Figure 5. Changes in IgM and IgG antibodies in the 105 asymptomatic individuals respectively on the twelfth day and the twenty-second day. A, Changes in IgM and IgG antibodies on the twelfth day; B, Changes in IgM and IgG antibodies on the twenty-second day.

HOW NANOPHOTONIC LABEL-FREE BIOSENSORS CAN CONTRIBUTE TO RAPID AND MASSIVE DIAGNOSTICS OF RESPIRATORY VIRUS INFECTIONS: COVID-19 CASE

Soler M, Estevez MC, Cardenosa-Rubio M, Astua A, Lechuga LM.. ACS Sens. 2020 Sep 25;5(9):2663-2678. doi: 10.1021/acssensors.0c01180. Epub 2020 Aug 24.
Level of Evidence: Other - Review / Literature Review

BLUF

A literature review, conducted by investigators from the Catalan Institute of Nanoscience and Nanotechnology (Spain), found that label-free nanophotonic biosensors may offer a combination of sensitivity, specificity, and speed that will allow for cheap, point-of-care testing of viral infections, such as those by SARS-CoV-2 (Figure 2, 3). While nanophotonic biosensors have demonstrated rapid sensitivity and specificity for different particles in academic settings, it is limited in use in the real world by the need to develop high-quality bioreceptors specific for SARS-CoV-2 or other viruses. Due to this, nanophotonic biosensors are not yet ready for deployment for SARS-CoV-2 detection, although they remain a potential, point-of-care diagnostic tool for the future.

ABSTRACT

The global sanitary crisis caused by the emergence of the respiratory virus SARS-CoV-2 and the COVID-19 outbreak has revealed the urgent need for rapid, accurate, and affordable diagnostic tests to broadly and massively monitor the population in order to properly manage and control the spread of the pandemic. Current diagnostic techniques essentially rely on polymerase chain reaction (PCR) tests, which provide the required sensitivity and specificity. However, its relatively long time-to-result, including sample transport to a specialized laboratory, delays massive detection. Rapid lateral flow tests (both antigen and serological tests) are a remarkable alternative for rapid point-of-care diagnostics, but they exhibit critical limitations as they do not always achieve the required sensitivity for reliable diagnostics and surveillance. Next-generation diagnostic tools capable of overcoming all the above limitations are in demand, and optical biosensors are an excellent option to surpass such critical issues. Label-free nanophotonic biosensors offer high sensitivity and operational robustness with an enormous potential for integration in compact autonomous devices to be delivered out-of-the-lab at the point-of-care (POC). Taking the current COVID-19 pandemic as a critical case scenario, we provide an overview of the diagnostic techniques for respiratory viruses and analyze how nanophotonic biosensors can contribute to improving such diagnostics. We review the ongoing published work using this biosensor technology for intact virus detection, nucleic acid detection or serological tests, and the key factors for bringing nanophotonic POC biosensors to accurate and effective COVID-19 diagnosis on the short term.

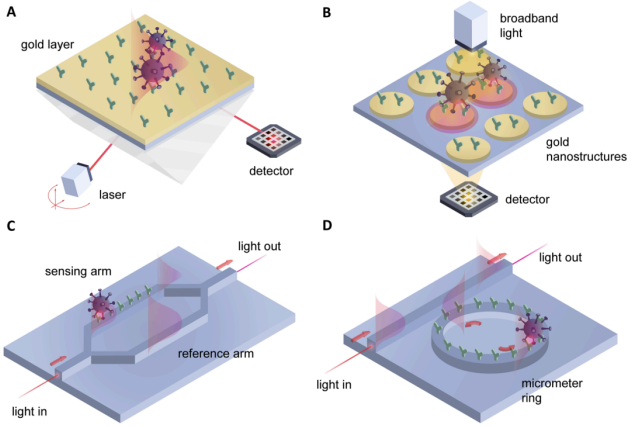

Figure 2. Schematic illustrations of the main label-free nanophotonic biosensor technologies: (A) Surface Plasmon Resonance (SPR) biosensor in Kretschmann configuration; (B) Localized Surface Plasmon Resonance (LSPR) biosensor based on gold nanodisks; (C) Mach–Zehnder
interferometric (MZI) biosensor; and (D) ring resonator biosensor.

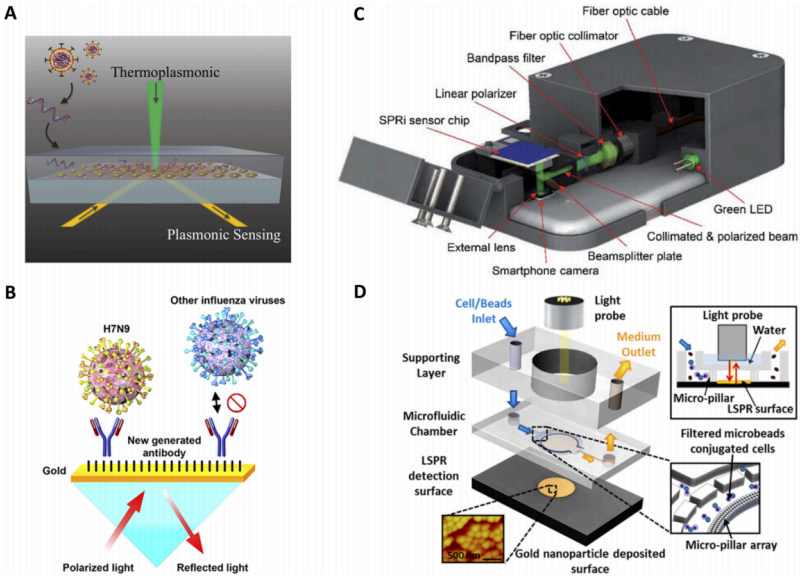

Figure 3. (A) Example of nanophotonic biosensor applied for COVID-19 diagnosis via genomic detection of SARS-CoV-2. Reprinted (adapted) with permission from ref 98. Copyright (2020) American Chemical Society. (B) Example of nanophotonic biosensor applied for direct detection of intact viruses (influenza). Reprinted (adapted) with permission from ref 104. Copyright (2018) American Chemical Society. (C) Example of smartphoneintegrated optical biosensor. Reprinted (adapted) with permission from ref 130. Copyright (2017) Elsevier. (D) Example of microfluidics-integrated optical biosensor. Reprinted (adapted) with permission from ref 134. Copyright (2014). American Chemical Society. Please refer to original articles for reprint.

ACKNOWLEDGEMENTS

CONTRIBUTORS

Eva Shelton
Krithika Kumarasan
Renate Meckl
Sameer Kandula
Tasha Ramparas
Tyler Gallagher
Veronica Graham
Zainab Awan

EDITORS

Alvin Rafou
Maggie Donovan
Michelle Arnold

SENIOR EDITORS

Allison Hansen
Avery Forrow
Cameron Richards
Sangeetha Thevuthasan

SENIOR EXECUTIVE EDITOR

Ann Staudinger Knoll

CHIEF EDITOR

Brennan Enright

ADVISOR

Will Smith