

The Daily COVID-19 Literature Surveillance Summary

November 05, 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.

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<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

Understanding the Pathology

- Do childhood vaccines help protect against SARS-CoV-2? A team of Egyptian virologists inoculated mice with common childhood vaccines (BCG, Pneumococcal, Rotavirus, Diphtheria, Tetanus, Pertussis, Hepatitis B, Haemophilus influenzae, Meningococcal, Measles, Mumps, and Rubella) and found [no evidence of cross-reacting antibodies against SARS-CoV-2 in serum](#) up to seven weeks post-vaccination, suggesting that if childhood vaccines provide protection against SARS-CoV-2, it may not be antibody mediated.

Transmission & Prevention

- How often are discharged patients re-testing positive for SARS-CoV-2? A review of 62 studies evaluating recurrence of SARS-CoV-2 viral RNA in discharged COVID-19 patients found that the proportion of patients with [re-positive RT-PCR ranged from 2.4% to 69.2%](#) across studies, occurring from 1-38 days after discharge, which was attributed to false-negative tests prior to discharge, false positive tests following discharge, reinfection, reactivation, and intermittent viral shedding.

Adjusting Practice During COVID-19

- What treatment options should physicians consider for patients with psoriasis? Following a literature review, dermatologists from Tehran, Iran recommend [not starting immunosuppressive drugs for psoriatic patients](#) due to an increased risk of acquiring COVID-19 and instead encourage initiating and continuing low-risk immunomodulating drugs as a safer modality.

R&D: Diagnosis & Treatments

- Is there a correlation between vitamin D levels and COVID-19 severity? A retrospective study conducted by various medical institutions in Tehran, Iran investigated 73 subjects with confirmed COVID-19 and found mean serum vitamin D (25[OH]D) concentrations were significantly lower in the deceased compared to discharged patients, and [higher 25\(OH\)D levels were associated with less extensive lung involvement](#), suggesting a potential correlation between vitamin D status and clinical course, extent of lung involvement, and patient outcome in COVID-19.
- What are potential therapies to improve immune reconstitution and decreased cytokine storm? A literature review conducted by hematologists in Chongqing, China assessed [delayed immune reconstitution \(IR\) and cytokine storm \(CS\) as obstacles in COVID-19 recovery](#) due to the delicate balance between strengthening and inhibiting the immune response at appropriate times, while also observing kinetic changes of lymphocytes and cytokines to guide rational therapies. Their findings suggest IR could potentially be improved with Thymosin alpha-1, while adoptive COVID-19-specific T-cells and CS may be suppressed with convalescent plasma, IL-6 blockade, mesenchymal stem cells, and corticosteroids.

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UNDERSTANDING THE PATHOLOGY

IN ANIMAL MODELS

COMMON CHILDHOOD VACCINES DO NOT ELICIT A CROSS-REACTIVE ANTIBODY RESPONSE AGAINST SARS-COV-2

Kandeil A, Gomaa MR, El Taweel A, Mostafa A, Shehata M, Kayed AE, Kutkat O, Moatasim Y, Mahmoud SH, Kamel MN, Shama NMA, El Sayes M, El-Shesheny R, Yassien MA, Webby RJ, Kayali G, Ali MA.. PLoS One. 2020 Oct 28;15(10):e0241471. doi: 10.1371/journal.pone.0241471. eCollection 2020.

Level of Evidence: 3 - Mechanism-based reasoning

BLUF

A team of Egyptian virologists inoculated mice with common childhood vaccines (BCG, Pneumococcal, Rotavirus, Diphtheria, Tetanus, Pertussis, Hepatitis B, Haemophilus influenzae, Meningococcal, Measles, Mumps, and Rubella) and found no evidence of cross-reacting antibodies against SARS-CoV-2 in serum up to seven weeks post-vaccination (Figure 2). Authors suggest if childhood vaccines provide protection against SARS-CoV-2, it may not be antibody mediated and further studies are needed to identify whether or not childhood vaccines protect against COVID-19 infections through other immune mechanisms.

ABSTRACT

Anecdotal evidence showed a negative correlation between Bacille Calmette-Guerin (BCG) vaccination and incidence of COVID-19. Incidence of the disease in children is much lower than in adults. It is hypothesized that BCG and other childhood vaccinations may provide some protection against SARS-CoV-2 infection through trained or adaptive immune responses. Here, we tested whether BCG, Pneumococcal, Rotavirus, Diphtheria, Tetanus, Pertussis, Hepatitis B, Haemophilus influenzae, Hepatitis B, Meningococcal, Measles, Mumps, and Rubella vaccines provide cross-reactive neutralizing antibodies against SARS-CoV-2 in BALB/c mice. Results indicated that none of these vaccines provided antibodies capable of neutralizing SARS-CoV-2 up to seven weeks post vaccination. We conclude that if such vaccines have any role in COVID-19 immunity, this role is not antibody-mediated.

FIGURES

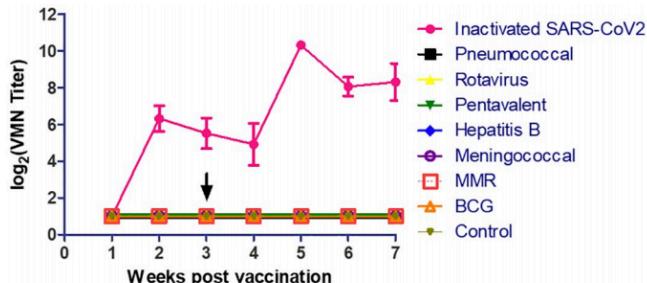


Fig 2. Weekly follow up of VMN titer against SARS-CoV-2 in immunized mice with most common childhood vaccines and inactivated SARS-CoV-2 vaccine.

TRANSMISSION & PREVENTION

DEVELOPMENTS IN TRANSMISSION & PREVENTION

RECURRENCE OF SARS-COV-2 VIRAL RNA IN RECOVERED COVID-19 PATIENTS: A NARRATIVE REVIEW

Dao TL, Hoang VT, Gautret P.. Eur J Clin Microbiol Infect Dis. 2020 Oct 28. doi: 10.1007/s10096-020-04088-z. Online ahead of print.

Level of Evidence: Other - Review / Literature Review

BLUF

Physicians from Aix Marseille University in France reviewed 62 studies evaluating recurrence of SARS-CoV-2 viral RNA in discharged COVID-19 patients (Table 1). The proportion of patients with re-positive RT-PCR ranged from 2.4% to 69.2% across studies, occurring from 1-38 days after discharge. Authors attribute re-positivity to false-negative tests prior to discharge, false positive tests following discharge, reinfection, reactivation, and intermittent viral shedding, suggesting that discharged patients should continue to take precautions until more studies can elucidate recovered patients' capacity to transmit COVID-19 following hospital discharge.

ABSTRACT

Many studies have shown that re-positive tests for SARS-CoV-2 by RT-PCR in recovered COVID-19 patients are very common. We aim to conduct this review to summarize the clinical and epidemiological characteristics of these patients and discuss the potential explanations for recurrences, the contagiousness of re-detectable positive SARS-CoV-2 virus, and the management of COVID-19 patients after discharge from hospital. The proportion of re-positive tests in discharged COVID-19 patients varied from 2.4 to 69.2% and persisted from 1 to 38 days after discharge, depending on population size, age of patients, and type of specimens. Currently, several causes of re-positive tests for SARS-CoV-2 in recovered COVID-19 patients are suggested, including false-negative, false-positive RT-PCR tests; reactivation; and re-infection with SARS-CoV-2, but the mechanism leading to these re-positive cases is still unclear. The prevention of re-positive testing in discharged patients is a fundamental measure to control the spread of the pandemic. In order to reduce the percentage of false-negative tests prior to discharge, we recommend performing more than two tests, according to the standard sampling and microbiological assay protocol. In addition, specimens should be collected from multiple body parts if possible, to identify SARS-CoV-2 viral RNA before discharge. Further studies should be conducted to develop novel assays that target a crucial region of the RNA genome in order to improve its sensitivity and specificity.

FIGURES

Table 1 (continued)											
Reference	Country	Population size	n (%) of re-detectable patients	Male gender n (%)	Age (years)	Type of sample	Time between discharge and re-positive test (days)	Serology	Symptoms during first episode	Symptoms during second episode	
[4]	China	-	4	30-36	Throat swabs	5-13	-	Mild to moderate	Asymptomatic		
[5]	France	-	11	6 (54.5%)	19-91	Respiratory samples	4-27	Serology was available in 9/11 patients. Of whom, 3 were negative, 4 were positive for IgG and IgM, 5 were positive for IgG only.	Mild to severe	3 deaths (54-, 72-, and 84-year-olds)	
[6]	China	126	3 (2.4%)	1 (33.3%)	60-76	Nasopharynx and oropharynx swabs	10-18	-	Asymptomatic		
[7, 8]	Korea	8922	292 (3.3%)	-	0-80	Respiratory samples	1-37	Serology was available in 23 patients. Of whom, 9/6% were positive for neutralizing antibodies	Asymptomatic		
[9]	China	651	23 (3.5%)	11 (48%)	27-89	Nasopharynx and oropharynx swabs	4-38	7 were positive for IgG and IgM for IgG only, and 11 were negative	Moderate to critical symptoms	15 (65%) were asymptomatic, 8 presented mild to moderate symptoms	
[10]	China	285	27 (9.5%)	12 (44.4%)	18-90	Nasopharyngeal swab	5-8	Serology was available in 20/27 patients. Of whom, 16 (80.0%) were positive for IgG and IgM	Mild (3, 11.5%), moderate (24, 88.9%)	Mild (20, 74.1%), moderate (7, 25.9%)	
[11]	China	576	61 (10.6%)	25 (41%)	<29-79	Nasal and pharyngeal swabs (36, 59%)	47 (77.0%)	Serology was available in 14/20 patients. Of whom, 13 (65.0%) had sputum (8, 13.1%), stool (7, 27.0%)	Mild (38, 62.5%), general (20, 32.8%), and severe (3, 4.9%)		
[12]	China	182	20 (11.0%)	13 (65.0%)	1-72	Nasopharyngeal swabs (14, 70%) and anal swabs (6, 30%)	13 (72.2%)	Serology was available in the 7th day and on the 7th day	Mild to moderate symptoms		
[13]	China	619	87 (14%)	45 (51.7%)	0-69	Nasopharyngeal swabs, throat swabs, and anal swabs	2-13	Serology was available in 59/87 patients. Of whom, 58 (98.3%) were positive for neutralizing antibody	Mild (46, 52.9%) and moderate (41, 47.1%)	Asymptomatic (77, 88.5%), mild (10, 11.5%)	
[14]	China	172	25 (14.5%)	8 (32.0%)	<12-60	Cloacal swab (56%) and nasopharyngeal swab (11, 44%)	7.32 ± 3.86	Non-severe (24, 96.0%), severe (1, 4.0%)	Asymptomatic (17, 68%) and mild cough (32.0%)		
[15]	China	66	11 (16.7%)	-	16-78	Stool specimen	-	Serology was available in 11/15 patients. Of whom, 11 (73.3%) had other symptoms (11/15, 73.3%), and other	Fever (12.5%, 80%), cough (11/15, 73.3%), and other (6.6% had dyspepsia)		
[16]	China	85	15 (17.6%)	4 (26.7%)	23-68	Rang =	Respiratory swabs	9-30	-	-	
[17]	China	70	15 (21.4%)	9 (60.0%)	Range = 51-73	Throat swab samples or nasal swab	-	-	-	-	
[18]	China	13	6 (46.2%)	6 (46.2%)	Range = 22-73	Fecal sample (2, 15.4%), sputum sample (4, 30.8%)	5-14	-	-	-	
[19]	Iran	13	9 (69.2%)	5 (55.6%)	Median = 52	Nasopharyngeal swabs	15-48	-	-	-	
[20]	Italy	1146	125 (10.9%)	61 (48.8%)	Mean = 65.7	Nasopharyngeal swabs	-	-	-	-	
[21]	China	108	8 (7.4%)	3 (37.5%)	26-72	Throat swab samples or nasal swab	6-28	Two patients (25.0%) had positive SARS-CoV-2 IgM, and all patients had positive SARS-CoV-2 IgG antibodies	Moderate (6, 75.0%) and severe (2, 25.0%)		
[22]	China	11	6 (54.5%)	4 (66.7%)	36-66	Oropharyngeal swab	6-27	Serology was available in 4 patients. Of whom, 4 (100%) were positive for IgG and IgM, and 2 (50%) was positive for IgM	Mild to moderate		
[23]	China	17	4 (23.5%)	2 (50.0%)	12-49	Nasopharyngeal swabs (2, 50%) anal swab (2, 50%)	3	-	-	Asymptomatic (1, 25.0%), mild (3, 75.0%)	
[24]	China	68	25 (36.8%)	10 (40.0%)	Mean = 47.6	Oropharyngeal swab	<7	IgM was positive in 4 (16.0%) and IgG positive in 19 (76.0%)	-	Asymptomatic and IgG positive (17, 68.0%), symptomatic (8, 32.0%)	
[25]	China	51	9 (17.6%)	-	-	Oropharyngeal swab	7-14	-	-	Asymptomatic (6, 64.3%), mild (3, 33.3%)	
[26]	China	15	1 (6.7%)	8 (53.3%)	9-62	Pharyngeal swab	15	-	-	Moderate (dyspnea)	
[27]	China	147	20 (13.6%)	12 (60.0%)	4-80	Pharyngeal swab	7-47	IgM and IgG were positive in 19 (95.0%) and negative in 1 (5.0%) of patients	-	Asymptomatic (12, 60.0%), severe (3, 15.0%), and critical (2, 10.0%)	
[28]	Bornei Darussalam	106	21 (19.8%)	12 (57.1%)	Mean = 47	Nasopharyngeal swabs	11-17	IgM and IgG were positive in 14 (66.7%) and negative in 7 (33.3%) of patients	-	Asymptomatic (20, 95.2%), mild (1, 4.8%)	
[29]	China	62	2 (3.2%)	1 (50.0%)	-	Pharyngeal swab	6-14	-	-	Mild	
[30]	China	20	3 (15.0%)	14 (70.0%)	23-57	Stool (3), saliva (2)	7	-	-	Asymptomatic	
[31]	China	98	17 (17.3%)	5 (29.4%)	Mean = 54	Sputum and nasopharyngeal swabs	<17	IgM was positive in 6 (35.3%) and negative in 11 (64.7%) of patients. IgG was positive in 7 (41.2%) and negative in 10 (58.8%)	-	Asymptomatic (5, 67.9%), severe (1, 15.2%), and negative in 17 (47.2%) patients. IgG was positive in 34 (94.4%) and negative in 2 (5.6%)	
[32]	China	257	53 (20.6%)	23 (43.4%)	29-87	Pharyngeal swab	1-12	-	-	General type (36, 67.9%), severe (5, 9.2%), and mild (1, 3.8%)	
[33]	China	161	22 (13.7%)	12 (54.5%)	Mean = 35.5	Nasal (3, 13.6%), pharyngeal (10, 45.4%), and anal (10, 45.4%) swabs	1-14	-	-	Asymptomatic (51, 67.9%), severe (1, 15.2%), and mild (1, 17.1%)	
[34]	China	37	5 (13.5%)	-	-	Pharyngeal swab	1-6	-	-	Mild to moderate	
[35]	China	55	5 (9.1%)	2 (40.0%)	27-42	Pharyngeal swab	4-17	-	-	Mild to moderate	
[36]	China	150	11 (7.3%)	6 (54.5%)	Median = 49	Pharyngeal swab	-	IgM was positive in 5 (45.5%) and IgG was positive in 11 (100%) patients	-	-	
[37]	China	14	7 (50.0%)	3 (42.9%)	2-7	Nasopharyngeal swab	7-17	-	-	Asymptomatic (2, 28.6%), moderate (5, 71.4%)	
[38]	Italy	29	6 (20.6%)	3 (50.0%)	37-78	Nasopharyngeal swab	13-24	-	-	Mild to moderate	
[39]	China	117	12 (10.3%)	6 (50.0%)	35-76	Pharyngeal swab and stool sample	-	-	-	Asymptomatic or mild	
[40]	China	71	19 (26.8%)	12 (63.2%)	18-71	Pharyngeal swab	1-17	IgM was positive in 8 (42.1%), IgG was positive in 19 (100%)	-	Mild (15, 78.9%), severe (4, 21.1%)	
[41]	China	62	15 (24.2%)	11 (73.3%)	34-77	Nasopharyngeal swab	-	-	-	Mild to severe	
[42]	China	133	22 (16.5%)	14 (63.0%)	2-64	Fecal and sputum samples	-	-	-	Mild (17, 77.3%), complicated illness (3, 13.6%), severe (1, 9.1%), and critical (2, 9.1%)	
[43]	China	-	1	1 (33.3%)	34	Oropharyngeal swab	15	IgM was negative and IgG was positive in all of three patients	-	Severe	
[44]	China	-	3	1 (33.3%)	34-74	Nasopharyngeal swabs	1-5	IgM was negative and IgG was positive in all of three patients	-	Mild	
[45]	China	-	1	1	70	Nasopharyngeal swabs	13	IgM and IgG were positive	-	Asymptomatic	
[46]	France	-	3	1 (33.3%)	84-90	Nasopharyngeal and sputum swabs	-	IgM and IgG were positive	-	Mild	All patients died
[47]	China	-	1	1	35	Nasopharyngeal swabs, sputum	14	IgM was negative and IgG was positive	-	Mild	
[48]	China	-	1	0	57	Nasopharyngeal swab	4	IgM was negative and IgG was positive	-	Mild	
[49]	Italy	-	1	1	48	Nasopharyngeal swab	30	IgM was negative and IgG was positive	-	Mild	

Table 1 (continued)

Reference	Country	Population size	n (%) of re-detectable patients	Male gender n (%)	Age (years)	Type of sample	Time between discharge and re-positive test (days)	Serology	Symptoms during first episode	Symptoms during second episode	
[50]	China	-	7	4 (57.1%)	< 67	Nasal and pharyngeal swabs	7-13	-	Mild to moderate	Asymptomatic	
[51]	China	-	1	1	54	Sputum	4	-	Moderate	Asymptomatic	
[52]	Brazil	-	1	1	26	Oropharyngeal and nasopharyngeal swabs	30	IgM and IgG were negative	Mild	Severe	
[53]	China	-	1	1	30	Nasopharyngeal swab	123	IgG was positive	Moderate	Asymptomatic	
[54]	China	-	1	1	40	Oropharyngeal swab	5	IgM and IgG were low positive	Severe	Severe	
[55]	China	7	6 (85.7%)	0-35	Pharyngeal (3) and rectal (5)	7-11	-	-	Mild (6, 85.7%), moderate (1, 14.3%)	Asymptomatic	
[56]	China	-	2	1 (50.0%)	21 and 55	Pharyngeal and anal swabs	17	-	Moderate	-	
[57]	China	-	6	0 (0%)	30-56	Respiratory samples	3-14	-	-	Asymptomatic (4, 66.6%), mild (1, 16.7%), and moderate (1, 16.7%)	
[58]	China	-	1	1	8	Pharyngeal swab	15	IgM and IgG were positive	Mild	Mild	
[59]	Korea	-	1	1	8	Respiratory samples	14	-	Mild	Mild	
[60]	Switzerland	-	2	0 (0)	81 and 77	Nasopharyngeal swab	14-21	-	Moderate	Moderate (1, 50.0%) and death (1, 50.0%)	
[61]	China	-	1	1	50	Nasopharyngeal swab	-	IgM and IgG were positive	Mild	Asymptomatic	
[62]	USA	-	1	1	82	-	10	-	Critical	Critical	
[63]	Italy	-	1	0	69	Nasopharyngeal swab	23	IgG was positive, IgM was negative	Mild	Asymptomatic	
[64]	Korea	-	1	0	72	Naso- and oropharyngeal swabs	6	-	Moderate	-	
[65]	China	-	1	0	46	Pharyngeal swab	6	-	Mild	Mild	

ANIMALS AND SARS-COV-2: SPECIES SUSCEPTIBILITY AND VIRAL TRANSMISSION IN EXPERIMENTAL AND NATURAL CONDITIONS, AND THE POTENTIAL IMPLICATIONS FOR COMMUNITY TRANSMISSION

Hobbs EC, Reid TJ.. Transbound Emerg Dis. 2020 Oct 22. doi: 10.1111/tbed.13885. Online ahead of print.

Level of Evidence: Other - Review / Literature Review

BLUF

This literature review conducted in October of 2020 by the Australian Center for Disease Preparedness found documentation of experimental and natural transmission of SARS-CoV-2 among various animals including mink, cats, ferrets, hamsters, bats, and non-human primates, whereas dogs, pigs, and poultry seemed to have limited to no susceptibility (Tables 1,2). Authors highlight a potential role for animals in community transmission of SARS-CoV-2 but suggest further surveillance and descriptive research to support these findings.

ABSTRACT

The current COVID-19 global pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) of probable bat origin, has highlighted the ongoing need for a One Health response to emerging zoonotic disease events. Understanding the human-animal interface and its relevance to disease transmission remains a critical control point for many emerging zoonoses. Determination of the susceptibility of various animal species to infection with SARS-CoV-2 and the role of animals in the epidemiology of the disease will be critical to informing appropriate human and veterinary public health responses to this pandemic. A scoping literature review was conducted to collect, evaluate and present the available research evidence regarding SARS-CoV-2 infections in animals. Experimental studies have successfully demonstrated SARS-CoV-2 infection and transmission in cats, ferrets, hamsters, bats and non-human primates under experimental settings. Dogs appear to have limited susceptibility to SARS-CoV-2, while other domestic species including pigs and poultry do not appear susceptible. Naturally occurring SARS-CoV-2 infections in animals appear uncommon, with 14 pets, 8 captive big cats and an unreported number of farmed mink testing positive to date. Infections typically appear asymptomatic in dogs, while clinical signs of respiratory and/or gastrointestinal disease tend to be mild to moderate in felines, and severe to fatal in mink. Most animals are presumed to have been infected by close contact with COVID-19 patients. In domestic settings, viral transmission is self-limiting, however in high density animal environments there can be sustained between-animal transmission. To date, two potential cases of animal-to-human transmission are being investigated, on infected mink farms. Given the millions of COVID-19 cases worldwide and ongoing potential for further zoonotic and anthroponotic viral transmission, further research and surveillance activities are needed to definitively determine the role of animals in community transmission of SARS-CoV-2.

FIGURES

Animal species	Clinical signs	Pathological changes on necropsy	Replication	Transmission to in-contact animals	Antibody response
Ferrets	+++	+++	+++	+++	+++
Cats	++	++	+++	+++	+++
Dogs	-	-	-	-	+
Hamsters	+	DU	+	++	++
Non-human primates	+	+++	++	++	++
Fruit bats	-	DU	++	++	++
Tree shrews	-	++	+	DU	DU
Chickens	-	-	-	-	-
Ducks	-	-	-	-	-

Extent of each characteristic is indicated by – (not seen), + (to some extent), ++ (to a moderate extent) or +++ (to a large extent).

DU: data unavailable

Table 1: Characteristics of animal species experimentally infected with SARS-CoV-2.

Animal species	PCR positive	Virus isolation positive	Antibody positive	Clinical signs observed	Confirmed link to human case	Total confirmed infections
						n
DOMESTIC						
Dogs	3	1 33%	3 100%	1 33%	3 100%	3
Cats	11	0 0%	2 18%	8 73%	8 73%	11
ZOO						
Tigers	5	DU DU	DU DU	4 80%	DU DU	5
Lions	3	DU DU	DU DU	3 100%	DU DU	3
FARMED						
Mink	19 [†]	DU DU	DU DU	6 [†] 32%	4 21%	19 [†]

[†]Number of infected farms. Number of animals not reported.

DU: data unavailable

Table 2: Summary data for all animal cases (as defined by positive PCR test) of SARS-CoV-2 infection to date.

ADJUSTING PRACTICE DURING COVID-19

MEDICAL SUBSPECIALTIES

DERMATOLOGY

IMMUNOSUPPRESSIVE DRUGS FOR PATIENTS WITH PSORIASIS DURING THE COVID-19 PANDEMIC ERA. A REVIEW

Sadeghinia A, Daneshpazhooh M.. Dermatol Ther. 2020 Nov 3. doi: 10.1111/dth.14498. Online ahead of print.

Level of Evidence: 1 - Review / Literature Review

BLUF

Dermatologists from Tehran, Iran conducted a literature review to provide recommendations on various immunosuppressive drugs for patients with psoriasis during the COVID-19 pandemic (Summary, Figure 1). In general, they recommend not starting immunosuppressive drugs for psoriatic patients due to an increased risk of acquiring COVID-19 and instead encourage initiating and continuing low-risk immunomodulating drugs as a safer modality.

SUMMARY

The recommendations of immunosuppressive drugs for psoriasis during the COVID-19 pandemic are as follows:

- Immunosuppressive drugs should be discontinued in those actively infected with COVID-19. Drugs such as Methotrexate, Cyclosporine, JAK-2 Inhibitors, and TNF-alpha inhibitors should not be initiated during the COVID-19 pandemic due to some increased risk of acquiring the COVID-19 infection.
- However, patients who have already been taking the drugs listed above and are not actively infected should continue their current regimen. Cessation of these drugs might increase the risk of recurrence of Psoriasis and Erythroderma.
- IL-17 and IL12/23 inhibitors are associated with lower risk of infections (may control the cytokine storm associated with COVID-19) and can be initiated or continued for treatment of Psoriasis.
- Patients with co-morbidities ("cardiovascular diseases, diabetes, hepatitis B, chronic obstructive pulmonary disease, chronic kidney diseases, and cancer") should switch to using systemic retinoids, Apremilast, and home phototherapy.

ABSTRACT

The COVID-19 has been spreading around the world. Concerns about the safety of administration of immunosuppressive drugs have been raised for treatment of psoriasis (PSO), and there is insufficient evidence for the risk of COVID-19 infection for psoriatic patients using these drugs, so we did a review, focusing on the risk of overall infection associated with the most commonly used immunosuppressive drugs such as methotrexate, biologics, cyclosporin, Janus kinase (JAK) inhibitors for the treatment of PSO. The data on the effect of immunosuppressive drugs on this virus may be ever-changing and remains to be clear. We recommend the initiation and continuation of low-risk immunomodulating drugs such as Interleukin (IL)-17, IL-12/23, and IL-23 inhibitors for treatment of PSO during COVID-19 era. For psoriatic patients with comorbidities switching to safer modalities such as systemic retinoids, apremilast, and home phototherapy is recommended. Immunosuppressive drugs should be withheld in psoriatic patients with the COVID-19 infection. This article is protected by copyright. All rights reserved.

FIGURES

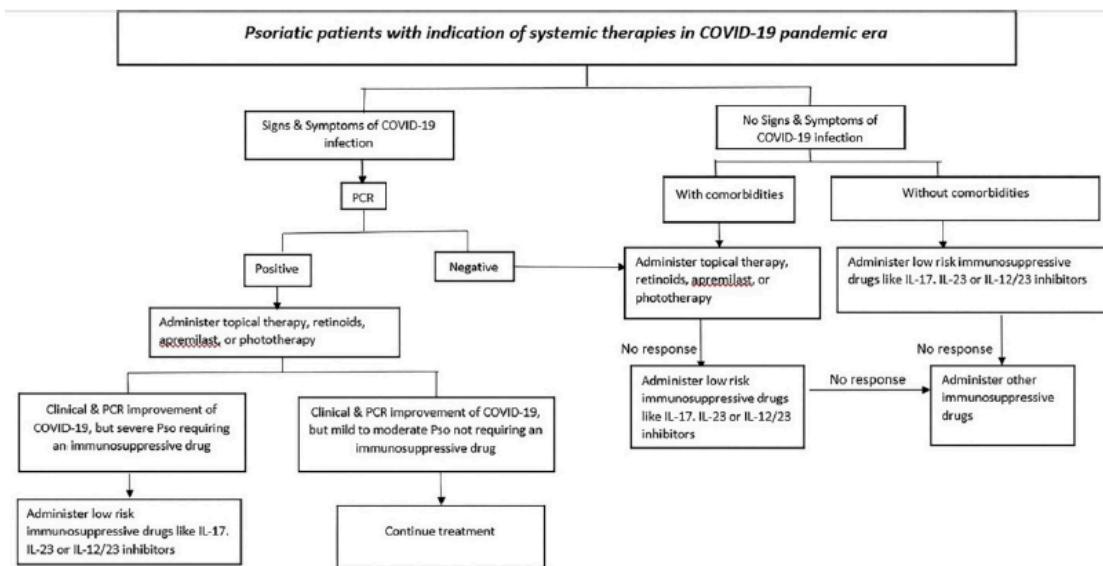


Figure 1: The proposed algorithm for management of patients with psoriasis requiring systemic treatments in COVID-19 pandemic era

R&D: DIAGNOSIS & TREATMENTS

DEVELOPMENTS IN DIAGNOSTICS

POSSIBLE ASSOCIATION OF VITAMIN D STATUS WITH LUNG INVOLVEMENT AND OUTCOME IN PATIENTS WITH COVID-19: A RETROSPECTIVE STUDY

Abrishami A, Dalili N, Mohammadi Torbati P, Asgari R, Arab-Ahmadi M, Behnam B, Sanei-Taheri M.. Eur J Nutr. 2020 Oct 30:1-9. doi: 10.1007/s00394-020-02411-0. Online ahead of print.

Level of Evidence: 4 - Local non-random sample

BLUF

A retrospective study conducted by various medical institutions in Tehran, Iran investigated 73 subjects with confirmed COVID-19 who were admitted between February and April of 2020. They found mean serum vitamin D (25[OH]D) concentration was significantly lower in the deceased compared to discharged patients (Table 2, Figure 3), and higher 25(OH)D levels were associated with less extensive lung involvement (Figure 2). These findings suggest potential correlation between vitamin D status and clinical course, extent of lung involvement, and patient outcome in COVID-19.

ABSTRACT

PURPOSE: Vitamin D deficiency has been reported as a key factor in the development of infectious diseases such as respiratory tract infections and inflammatory processes like acute respiratory distress syndrome. However, the impact of vitamin D on the severity and outcome of COVID-19 is still not fully known. Herein, we aimed to evaluate the prognostic role of serum vitamin D concentration on the extent of lung involvement and final outcome in patients with COVID-19. **METHODS:** Seventy-three subjects with confirmed diagnosis of COVID-19 were investigated in this study. The patients had been admitted to our academic hospital from February 28, 2020 to April 19, 2020. Demographic and clinical data, serum 25(OH)D levels, and findings of initial chest computed tomography were recorded. Linear and binary logistic regression, cox regression and ROC curve tests were used for statistical analysis. **RESULTS:** The mean age of patients was 55.18 ± 14.98 years old; 46.4% were male. Mean serum 25(OH)D concentration was significantly lower in the deceased (13.83 ± 12.53 ng/ mL compared with discharged patients (38.41 ± 18.51 ng/mL) ($P < 0.001$). Higher levels of 25(OH)D were associated with significantly less extent of total lung involvement (beta = - 0.10, $P = 0.004$). In addition, vitamin D deficiency [25(OH) D < 25 ng/mL] was associated with a significant increase in the risk of mortality (hazard ratio = 4.15, $P = 0.04$). **CONCLUSION:** This study suggests that serum vitamin D status might provide useful information regarding the clinical course, extent of lung involvement and outcome of patients with COVID-19. However, further studies with larger sample size are needed to confirm these findings.

FIGURES

Table 2. Multivariate linear regression results in the association of 25(OH) D concentration and lung involvement scores

Variables	Upper Zone		Middle zone		Lower zone		Total	
	β (SE)	P	β (SE)	P	β (SE)	P	β (SE)	P
25(OH) D*	- 0.04 (0.011)	0.003	- 0.04 (0.012)	0.003	- 0.03 (0.014)	0.02	- 0.11 (0.034)	0.003
Age	0.02 (0.014)	0.29	0.03 (0.015)	0.038	0.04 (0.018)	0.04	0.08 (0.042)	0.05
Sex (male)	0.79 (0.44)	0.08	0.67 (0.47)	0.16	- 0.55 (0.56)	0.33	0.91 (1.34)	0.50
Comorbidity (yes)	0.78 (0.42)	0.07	1.09 (0.45)	0.018	0.68 (0.54)	0.21	2.55 (1.28)	0.05
25(OH) D**	- 0.03 (0.011)	0.003	- 0.03 (0.012)	0.005	- 0.04 (0.014)	0.01	- 0.10 (0.034)	0.004

*Unadjusted multivariate model

**Adjusted multivariate model

Table 2. Multivariate linear regression results in the association of 25(OH) D concentration and lung involvement scores

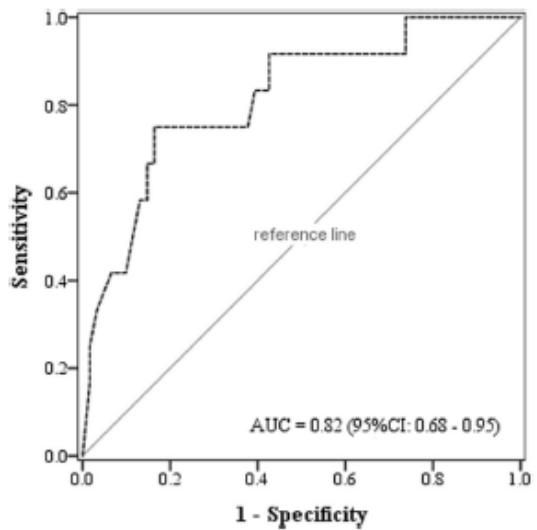


Fig. 3 ROC curve analysis results to achieve predictive values of 25(OH)D in classifying patients into dead or discharge

Figure 3. ROC curve analysis results to achieve predictive values of 25(OH)D in classifying patients into dead or discharge

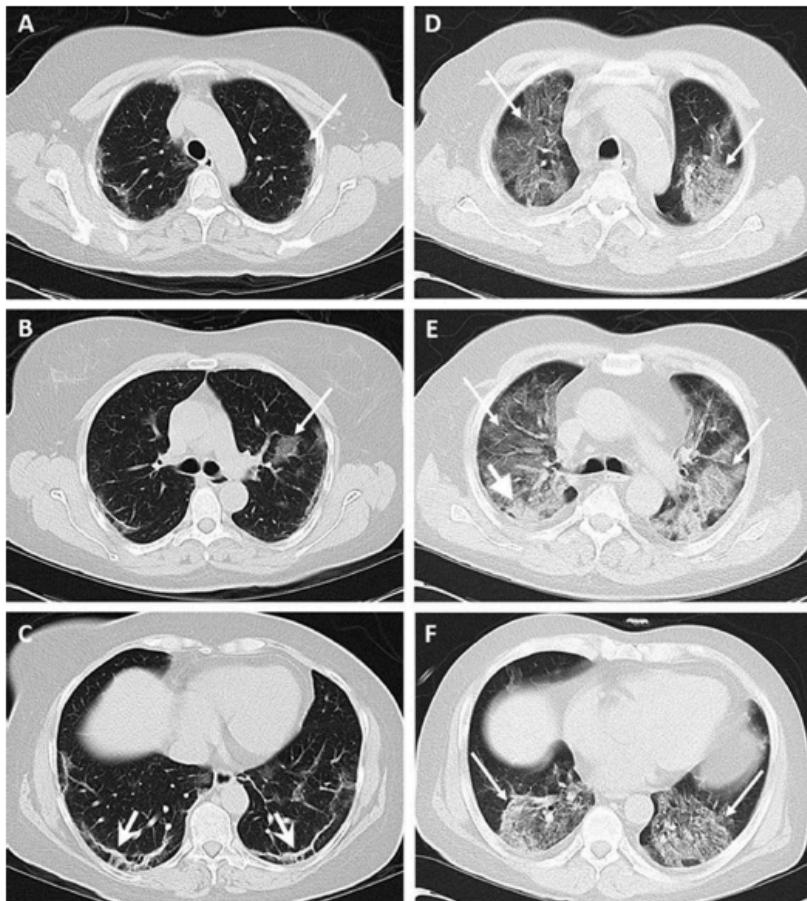


Fig. 2 **a-c** A 55-year-old man presented with 5-day history of fever and dry cough without any comorbidity [25(OH)D level was 40 ng/mL] with initial lung computed tomography (CT) involvement score of eight/24. On admission, CT images showed subtle patchy ground-glass opacities (GGO) (long arrows) predominantly in upper zones and reticular pattern (wide arrows) in lower zones. The patient dis-

charged after 6 days. **d-f** A 54-year-old man presented with 4-day history of fever, dry cough and dyspnea and no other comorbidity [25(OH)D level was 7 ng/mL]. Lung CT score involvement score of ninety/24. On admission, CT images showed diffuse GGO (long arrows) with slight consolidation change (thick head arrow) in right mid zone. The patient died after 19 days

OPTICAL BIOSENSORS FOR VIRUS DETECTION: PROSPECTS FOR COVID-19

Maddali H, Miles CE, Kohn J, O'Carroll DM.. Chembiochem. 2020 Oct 29. doi: 10.1002/cbic.202000744. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Chemists from Rutgers University in New Jersey reviewed potential utility of optical biosensors for SARS-CoV-2 testing by outlining various techniques (i.e. fluorescence, plasmon enhanced fluorescence, surface enhanced Raman scattering, colorimetry, surface plasmons), previous application for detection of other viruses (i.e. Ebola, HIV), and current literature demonstrating optical biosensor capacity to detect specific SARS-CoV-2 antibodies and sequences (Table 1, Figure 2). Authors suggest fluorescence techniques with good reproducibility, high selectivity, and advanced design are suitable alternatives to current RT-PCR tests, which require more advanced training and multiple steps.

ABSTRACT

The recent pandemic of the novel coronavirus disease 2019 (COVID-19) caused massive worldwide disruptions due to the lack of available testing locations and equipment. The use of optical techniques for viral detection has flourished in the past 15 years, providing more reliable, inexpensive, and accurate detection methods. In the current minireview, optical phenomena including fluorescence, surface plasmons, surface-enhanced Raman scattering (SERS), and colorimetry are discussed in the context of detecting virus pathogens. The sensitivity of a viral detection method can be dramatically improved by utilizing materials that exhibit surface plasmons or SERS, but often it requires advanced instrumentation for detection. Although fluorescence and colorimetry lack high sensitivities, they show promise as point-of-care diagnostics because of their relatively less complicated instrumentation, ease of use, lower costs, and they do not require nucleic acid amplification. Advantages and disadvantages of each optical detection method are presented, and prospects for applying optical biosensors in COVID-19 detection are discussed.

FIGURES

Method	Virus	Detection Element	Detection Limit	Reference
Fluorescence	Dengue	Immunofluorescence-assay detecting sandwich complex of antibody conjugated silica microbead and fluorescently labeled dual antibody	1×10^4 PFU/mL	[80c]
	HIV or Hepatitis B	Microbeads optically barcoded by CdSeS QDs coated with capture DNA adhered to a chip	1×10^3 copies/mL	[91]
	Avian Influenza H9N2	Antibody conjugated fluorescent nanobioprobes coupled with antibody conjugated immunomagnetic beads to create fluorescent-biotargeting bifunctional cells	8.94×10^6 fg/mL	[92]
	Influenza (H1N1 DNA)	Sandwich complex between a CdTe QD and a protein binding aptamer further amplified with streptavidin	3.45×10^6 fM	[93]
Plasmon Enhanced Fluorescence	Ebola	Hybrid microfluid and optofluidic device with target RNA functionalized magnetic microbeads	0.2 PFU/mL	[80b]
	Avian Influenza H5N1 (rHA protein)	Influenza aptamers immobilized on AgNPs forming a complex with thiazole orange in the presence of rHA protein	3.5×10^6 fg/mL	[94]
	Influenza	Conjugation of fluorescent QDs, AuNPs, and virus antibodies to peptide linker	17.02 fg/mL	[86]
	Influenza (H1N1 and H3N2)	Binding of antibody conjugated AuNPs and CdSeTeS QDs to virus particles	H1N1: 30 fg/mL (water), 4 x 10^5 fg/mL (human serum) H3N2: 10 PFU/mL	[95]
	Norovirus	Norovirus antibody attached to a biosensor chip with QD antigens	1×10^4 fg/mL (4.3×10^5 copies/mL)	[52]

Table 1. Different optical techniques used to detect various viruses

SARS-CoV	Fluorescently labeled antibodies attached to AuNPs	1×10^2 fg/mL	[96]	
Ebola	Antiviral immunoglobulins attached to a protein surface coating on a gold layer nanoplasmonic sensor	1×10^5 PFU/mL	[97]	
Dengue	Surface activation of antigens on a gold chip to attract and covalently couple virus antibodies	1 uL sample	[98]	
Dengue	Antibody modified polymer sensor film to bind virus proteins	8×10^4 fM	[54]	
SPR	HIV DNA	DNA conjugated AgNPs to sandwich HIV DNA forming an agglomerate	1.95×10^5 fM	[53]
Hepatitis B (surface antibody)	Hepatitis B surface antibody imprinted on polymer film on a SPR sensor	208.2 mIU/mL	[99]	
Hepatitis B (surface antigen)	Hepatitis B surface antigen bound to SPR sensor	7.81 fg/mL	[80a]	
Avian Influenza H5N1	Biotinylated aptamers immobilized on a streptavidin modified gold surface	0.128 HAU	[100]	
Hepatitis B (DNA representative)	DNA-capture strand coupled to DNA-reporter strand labeled with a Raman reporter on free AuNPs	0.44 fM	[80d]	
Rift valley fever virus (RVFV)	Raman reporter coated AuNPs sandwich the virus with antibody conjugated para magnetic NPs	5 fg/mL	[64b]	
Respiratory Syncytial	Citrate capped AgNPs that aggregate with an RSV-antibody sandwich complex	50 fg/mL	[88]	
Dengue, Yellow Fever, Ebola	Sandwich hybridization between multicolored antibody-AuNPs, virus particle, and surface adhered antibodies on a flow device	1.5×10^8 fg/mL (all)	[71]	
Hepatitis B and C	Chip with DNA hybridized AuNPs, enhanced with silver staining	3.6×10^4 fM; Hepatitis C: 3.6×10^5 fM	[101]	
Influenza A (H3N2)	Color change induced by antibody conjugated AuNPs attaching to virus receptor probes	7.8 HAU	[102]	
Colorimetry	Influenza	Antibody conjugated AuNPs and biotinylated aptamer binding with virus particles on a Dual recognition element LFA	2×10^6 copies/mL	[103]
Avian Influenza (H5N3, H7N1, H9N2)	Lateral flow immunoassay with latex particles conjugated with influenza antibody and surface adhered influenza antibodies	H5N3: 6.25×10^5 PFU/mL; H7N1: 5.34×10^5 PFU/mL; H9N2: 1.37×10^5 PFU/mL	[38]	
Zika	Amplified nucleic acids detected with leuco crystal violet on a microfluidic chip	5 PFU/mL	[104]	

Table 1. continued.

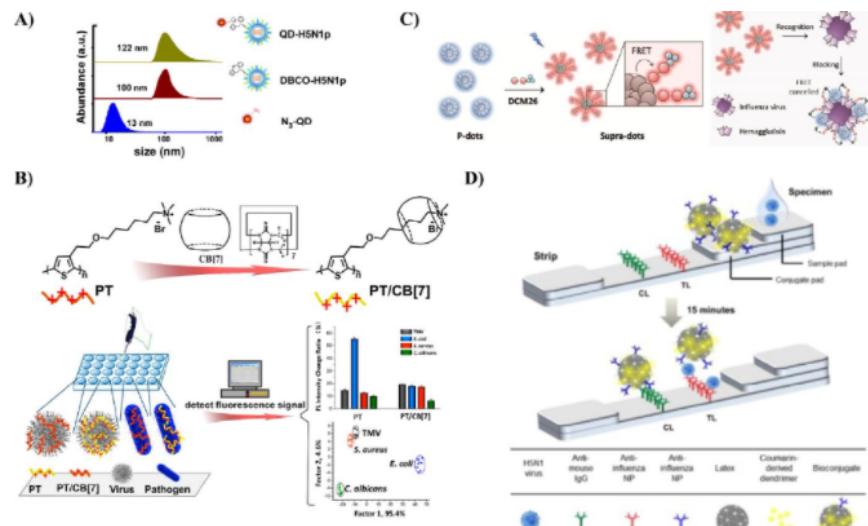


Figure 2. Fluorescence techniques for virus detection. A) Bioorthogonal labeling of H5N1p with NIR QDs for a noninvasive detection method. Reproduced with permission from Pan *et al.*^[19a] B) PT and PT/CB[7] synthesis to form a supramolecular structure with TMV and other pathogens resulting in a change in fluorescence intensity. Reproduced with permission from Bai *et al.*^[4] C) Formation of supra-dots from p-dots and DCM dye molecules causing a decrease in FRET signal when the supra-dots bind to the hemagglutinin of influenza virus. Reproduced with permission from Wang *et al.*^[37] D) Fluorescence detector flow strip using antibodies to capture antibody conjugated latex NPs for the detection of influenza virus. Reproduced with permission from Yeo *et al.*^[38]

DEVELOPMENTS IN TREATMENTS

T-CELL IMMUNOBIOLOGY AND CYTOKINE STORM OF COVID-19

Luo XH, Zhu Y, Mao J, Du RC.. Scand J Immunol. 2020 Oct 28:e12989. doi: 10.1111/sji.12989. Online ahead of print.

Level of Evidence: Other - Review / Literature Review

BLUF

A literature review conducted by hematologists in Chongqing, China assessed delayed immune reconstitution (IR) and cytokine storm (CS) as obstacles in COVID-19 recovery due to the delicate balance between strengthening and inhibiting the immune response at appropriate times, while also observing kinetic changes of lymphocytes and cytokines to guide rational therapies (Figure 1). Their findings suggest IR could potentially be improved with Thymosin alpha-1, while adoptive COVID-19-specific T-cells and CS may be suppressed with convalescent plasma, IL-6 blockade, mesenchymal stem cells, and corticosteroids. Authors highlight potential for checkpoint inhibitors in COVID-19 therapy, urging for further data on T-cell immunobiology.

ABSTRACT

2019 coronavirus disease (COVID-19) presents as a newly recognized pneumonia and could rapidly progress into acute respiratory distress syndrome which has brought about a global pandemic. Until now, no curative therapy has been strongly recommended for COVID-19 except for personalized supportive care. T cells and virus-specific T cells are essential to protect against virus infection, including COVID-19. Delayed immune reconstitution (IR) and cytokine storm (CS) remain serious obstacles for the cure of COVID-19. Most COVID-19 patients, especially among elderly patients, had marked lymphopenia and increased neutrophils, but T cell counts in severe COVID-19 patients surviving the disease gradually restored later. Elevated pro-inflammatory cytokines, particularly IL-6, IL-10, IL-2, and IL-17, and exhausted T cells are found in peripheral blood and the lungs. It suggests that Thymosin alpha1 and adoptive COVID-19-specific T cells could improve IR while convalescent plasma, IL-6 blockade, mesenchymal stem cells, and corticosteroids could suppress CS. More clinical studies in this field worldwide are urgently warranted to pave the way for therapy of COVID-19 in the future.

FIGURES

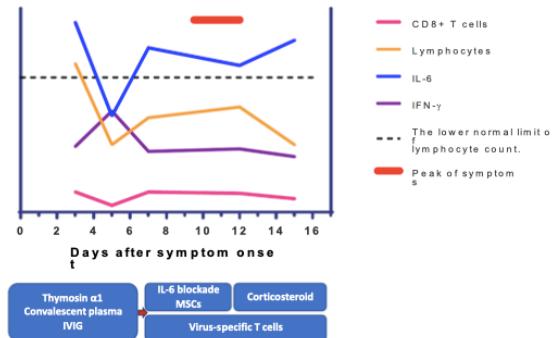


Figure 1: T-cell immune reconstitution and kinetics of cytokines in one patient who progresses to severe COVID-19 during a typical course. Proposed algorithm for improving IR and resolving CS. IVIG, Intravenous immunoglobulin; MSCs, Mesenchymal stem cells; IR, immune reconstitution; CS, cytokine storm.

FAVIPIRAVIR AS AN ANTIVIRAL AGENT IN COVID-19: SAME SCRIPT, DIFFERENT CAST?

Dauby N.. Clin Infect Dis. 2020 Oct 19:ciaa1600. doi: 10.1093/cid/ciaa1600. Online ahead of print.

Level of Evidence: Other - Opinion

BLUF

In this letter to the editor, a physician-scientist from the Department of Infectious Diseases at Université Libre de Bruxelles in Belgium discussed Favipiravir as a treatment for moderate severity COVID-19 infection in Russia, arguing the possible approval is premature given lack of data supporting its efficacy. The author suggests treatments for COVID-19, including Favipiravir, should not be promoted until repeated studies convincingly show beneficial outcomes such as reduced mortality or decreased intensive care unit transfer rates.

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