Daily COVID-19 Literature Surveillance

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Isolation and Rapid Sharing of the 2019 Novel Coronavirus (SAR-CoV-2) From the First Patient Diagnosed With COVID-19 in Australia

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Abstract

Objectives: To describe the first isolation and sequencing of SARS-CoV-2 in Australia and rapid sharing of the isolate.

Setting: SARS-CoV-2 was isolated from a 58-year-old man from Wuhan, China who arrived in Melbourne on 19 January 2020 and was admitted to the Monash Medical Centre, Melbourne from the emergency department on 24 January 2020 with fever, cough, and progressive dyspnoea.

Major outcomes: Clinical course and laboratory features of the first reported case of COVID-19 (the illness caused by SARS-CoV-2) in Australia; isolation, whole genome sequencing, imaging, and rapid sharing of virus from the patient.

Results: A nasopharyngeal swab and sputum collected when the patient presented to hospital were each positive for SARS-CoV-2 (reverse transcription polymerase chain reaction). Inoculation of Vero/hSLAM cells with material from the nasopharyngeal swab led to the isolation of SARS-CoV-2 virus in culture. Electron microscopy of the supernatant confirmed the presence of virus particles with morphology characteristic of viruses of the family Coronaviridae. Whole genome sequencing of the viral isolate and phylogenetic analysis indicated the isolate exhibited greater than 99.99% sequence identity with other publicly available SARS-CoV-2 genomes. Within 24 hours of isolation, the first Australian SARS-CoV-2 isolate was shared with local and overseas reference laboratories and major North American and European culture collections.

Conclusions: The ability to rapidly identify, propagate, and internationally share our SARS-CoV-2 isolate is an important step in collaborative scientific efforts to deal effectively with this international public health emergency by developing better diagnostic procedures, vaccine candidates, and antiviral agents.

Chloroquine in COVID-19: the evidence.

PMID: 32231349Apr 2, 2020

Gupta, Nitesh; Agrawal, Sumita; Ish, PranavMonaldi Arch Chest Dis

Key point: “The published literature till date has been summarised in the Table 1 below. The interim con- clusions from the published literature is that there is no current evidence of use of chloroquine for treatment of COVID-19. The use should be restricted to clinical trials with strict vigilance and follow up to further clarify the role. As of date 23 clinical trials are underway [2], only after the results of which, can the role of chloroquine in management of COVID-19 be decided. “

Table 1. Summary of trials/studies published on role of chloroquine in COVID-19.

Study	Patient	Intervention	Comparator	Outcome	Caveat
Letter to Editor [3]	>100 patients. Study done in China	Chloroquine, dose not mentioned	Not known	The statement reads as "treatment in inhibiting the exacerbation of pneumonia, improving lung imaging findings, promoting a virus-negative conversion, and shortening the disease course according to the news briefing." Thus, no specific primary or secondary end-points	No clinical details of any patient or outcome mentioned for readers/reviewers to analyse
Letter to Editor [4]	*In vitro* study	Remdesivir and chloroquine	Not known	*In vitro* inhibition	*In vitro* data should not be extrapolated to human beings without being tested
Commentary [5]	Not applicable	Not applicable	Not applicable	Not applicable	Use to be evaluated with promising announcements and potential detrimental effects observed in previous attempt to treat viral illness
Expert consensus [6]	Age >18 years and <65 years. (1) Mild: clinical symptoms are mild, and no pneumonia manifestations on imaging. (2) Ordinary type: with fever, respiratory tract symptoms, etc., imaging shows pneumonia. (3) Heavy: Meet any of the following: i) Respiratory distress, breathing rate >30 times/min; ii) In resting state, means oxygen saturation <93%; iii) Arterial partial pressure of oxygen (PaO_2) / inhaled oxygen concentration (FiO_2) <300 mmHg (1 mmHg = 0.133kPa).	Chloroquine phosphate tablet, at a dose of 500 mg twice per day for 10 days	Not applicable	During the course of treatment, if the nucleic acid of the throat swab becomes negative and is negative for 3 days, the drug withdrawal can be considered, but the minimum course of treatment needs 5 days. DISCHARGE: When the body temperature has returned to normal for more than 3 days, the respiratory symptoms have improved significantly, pulmonary imaging has shown significant inflammation absorption, and two consecutive respiratory pathogen nucleic acid tests negative (sampling interval of at least 1day), can be released from hospital or transferred to the appropriate department for other diseases according to the condition.	Adverse reactions, drug interactions, frequent electrocardiogram, hemogram, ophthalmology monitoring and mental status changes. Antibiotics such as quinolones and macrolides are forbidden

COVID-19 and chronological aging: senolytics and other anti-aging drugs for the treatment or prevention of corona virus infection?

PMID: 32229706Apr 2, 2020
Sargiacomo, Camillo; Sotgia, Federica; Lisanti, Michael PAging (Albany NY)
Full TextMechanismTreatment

COVID-19, also known as SARS-CoV-2, is a new emerging zoonotic corona virus of the SARS (Severe Acute Respiratory Syndrome) and the MERS (Middle East Respiratory Syndrome) family. COVID-19 originated in China and spread world-wide, resulting in the pandemic of 2020. For some reason, COVID-19 shows a considerably higher mortality rate in patients with advanced chronological age. This begs the question as to whether there is a functional association between COVID-19 infection and the process of chronological aging. Two host receptors have been proposed for COVID-19. One is CD26 and the other is ACE-2 (angiotensin-converting enzyme 2). Interestingly, both CD26 and the angiotensin system show associations with senescence. Similarly, two proposed therapeutics for the treatment of COVID-19 infection are Azithromycin and Quercetin, both drugs with significant senolytic activity. Also, Chloroquine-related compounds inhibit the induction of the well-known senescence marker, Beta-galactosidase. Other anti-aging drugs should also be considered, such as Rapamycin and Doxycycline, as they behave as inhibitors of protein synthesis, blocking both SASP and viral replication. Therefore, we wish to speculate that the fight against COVID-19 disease should involve testing the hypothesis that senolytics and other anti-aging drugs may

have a prominent role in preventing the transmission of the virus, as well as aid in its treatment. Thus, we propose that new clinical trials may be warranted, as several senolytic and anti-aging therapeutics are existing FDA-approved drugs, with excellent safety profiles, and would be readily available for drug repurposing efforts. As Azithromycin and Doxycycline are both commonly used antibiotics that inhibit viral replication and IL-6 production, we may want to consider this general class of antibiotics that functionally inhibits cellular protein synthesis as a side-effect, for the treatment and prevention of COVID-19 disease.

Intranasal corticosteroids in allergic rhinitis in COVID-19 infected patients: An ARIA-EAACI statement.

PMID: 32233040Apr 2, 2020

Bousquet, Jean; Akdis, Cezmi; Jutel, Marek; Bachert, Claus; Klimek, Ludger; Agache, Ioana; Ansotegui, Ignacio J; Bedbrook, Anna; Bosnic-Anticevich, Sinthia; Canonica, Giorgio W; Chivato, Tomas; Cruz, Alvaro A; Czarlewski, Wienia; Del Giacco, Stefano; Du, Hui; Fonseca, Joao A; Gao, Yadong; Haahtela, Tari; Hoffmann-Sommergruber, Karin; Ivancevich, Juan C; Khaltaev, Nikolai; Knol, Edward F; Kuna, Piotr; Larenas-Linnemann, Desiree; Mullol, Joaquim; Naclerio, Robert; Ohta, Ken; Okamoto, Y; O'Mahony, Liam; Onorato, Gabrielle L; Papadopoulos, Nikos G; Pfaar, Oliver; Samolinski, Boleslaw; Schwarze, Jurgen; Toppila-Salmi, Sanna; Teresa Ventura, Maria; Valiulis, Arunas; Yorgancioglu, Arzu; Zuberbier, TorstenAllergy

With the current knowledge, in patients with COVID-19 infection, intra-nasal corticosteroid (including spray) can be continued in allergic rhinitis at the recommended dose
Stopping local intra-nasal corticosteroid is not advised. Suppression of the immune system has not been proven and more sneezing after stopping means more spreading of the Corona virus
These recommendations are conditional since there is a paucity of data and they should be revised regularly with new knowledge

Perspectives on therapeutic neutralizing antibodies against the Novel Coronavirus SARS-CoV-2.

PMID: 32226289Apr 1, 2020

Zhou, Guangyu; Zhao, QiInt J Biol Sci

"The simplest and most direct approach to combating SARS-CoV-2 during the outbreak would be to use plasma from the convalescent patients [48]. Polyclonal NAbs could be induced in some convalescent patients and will be effective in treating SARS-CoV-2 [12]. These NAbs can provide passive immune responses to viral infection. Indeed, both SARS and Ebola patients received the treatment of convalescent plasma [49,50]. However, the outcomes of passive plasma therapy are unpredictable due to variability of sera in different patients.

Development of NAbs against SARS-CoV-2 is a relatively rapid approach to obtain the standardized agents that control re-emergence of COVID-19 [51]."

Table 1. Continued from previous page.

Study	Patient	Intervention	Comparator	Outcome	Caveat
Dutch CDC [7] **Currently, the document has been removed from the source**	Severe infections requiring admission to the hospital and oxygen therapy or admitted to the ICU	The suggested regimen in adults- 600 mg of chloroquine base followed by 300 mg after 12 h on day 1, then 300 mg/day on days 2-5 days	Not applicable	Not applicable	This document also underlined 1) the needs for stopping thetreatment at day 5 to reduce the side effects, considering the long half-life (30 hours); 2) the need to differentiate betweenchloroquine phosphate and chloroquine base since 500 mg of the first correspond to 300 mg of the second
Italian Society of Infectious and Tropical Diseases [8] **The document is currently inaccessible**	Italian Society of Infectious and Tropical disease (Lombardy section)	Chloroquine 500 mg/day or hydroxychloroquine 200 mg for 10 days, although the treatment may vary from 5 to 20 days according to clinical severity	The document is currently inaccessible	The document is currently inaccessible	The document is currently inaccessible
France [9]	Open label non-randomized clinical trial	Confirmed COVID-19 in a single arm protocol from early March to March 16th, to receive 600 mg of hydroxychloroquine daily and their viral load in nasopharyngeal swabs was tested daily in a hospital setting. Depending on their clinical presentation, azithromycin was added to the treatment	Untreated patients from another center and cases refusing the protocol were included as negative controls. **Presence and absence of virus at Day 6-post inclusion was considered the end point**	Viral load concentration was the end point. However, no mention of clinical outcomes mentioned	No clinical rationale of when and why did they decide the azithromycin to be added. Also, if the supplementary table is analysed the patients on chloroquine event showed increase in viral load on the contrary

Coronavirus Disease 19 Infection Does Not Result in Acute Kidney Injury: An Analysis of 116 Hospitalized Patients from Wuhan, China.

PMID: 32229732Apr 2, 2020

Wang, Luwen; Li, Xun; Chen, Hui; Yan, Shaonan; Li, Dong; Li, Yan; Gong, ZuojiongAm J Nephrol

Abstract

Background: Whether the patients with coronavirus disease 19 (COVID-19) infected by severe acute respiratory syndrome (SARS)-CoV-2 would commonly develop acute kidney injury (AKI) is an important issue worthy of clinical attention. This study aimed to explore the effects of SARS-CoV-2 infection on renal function through analyzing the clinical data of 116 hospitalized COVID-19-confirmed patients. ***Methods:*** One hundred sixteen COVID-19-confirmed patients enrolled in this study were hospitalized in the Department of Infectious Diseases, Renmin Hospital of Wuhan University from January 14 to February 13, 2020. The recorded information includes demographic data, medical history, contact history, potential comorbidities, symptoms, signs, laboratory test results, chest computer tomography scans, and treatment measures. SARS-CoV-2 RNA in 53 urine sediments of enrolled patients was detected by real-time reverse transcription-polymerase chain reaction. ***Results:*** Twelve (10.8%) patients showed mild increase of blood urea nitrogen or creatinine (<26 μmol/L within 48 h), and 8 (7.2%) patients showed trace or 1+ albuminuria in 111 COVID-19-confirmed patients without chronic kidney disease (CKD). All these patients did not meet the diagnostic criteria of AKI. In addition, 5 patients with CKD who were undergone regular continuous renal replacement therapy (CRRT) before admission were confirmed infection of SARS-CoV-2 and diagnosed as COVID-19. In addition to therapy for COVID-19, CRRT was also applied 3 times weekly during hospitalization for these 5 patients with CKD. In the course of treatment, the renal function indicators showed stable state in all 5 patients with CKD, without exacerbation of CKD, and pulmonary inflammation was gradually absorbed. All 5 patients with CKD were survived.

Moreover, SARS-CoV-2 RNA in urine sediments was positive only in 3 patients from 48 cases without CKD, and 1 patient had a positive for SARS-CoV-2 open reading frame 1ab from 5 cases with CKD. ***Conclusion:*** AKI was uncommon in COVID-19. SARS-CoV-2 infection does not result in AKI, or aggravate CKD in the COVID-19 patients.

COVID-19-confirmed patients (n = 116)	Number	BUN, mmol/L 3.6–9.5	SCr, μmol/L 57–111	eGFR, mL/min >90
Without CKD				
1st week	111	5.23±1.72	78.26±25.14	129.81±10.33
2st week	108	5.58±2.44	75.31±23.52	126.37±9.72
3st week	105	5.04±1.96	77.04±22.27	128.53±9.29
4st week	104	5.19±2.07	72.95±24.83	127.96±9.65
p value		0.877	0.121	0.177
With CKD				
1st week	5	32.08±8.58	937.61±114.62	14.43±7.34
2st week	5	30.66±9.64	955.47±141.09	15.96±8.72
3st week	5	29.79±10.37	897.53±175.48	21.33±10.09
4st week	5	31.94±9.18	914.29±163.87	22.86±9.37
p value		0.981	0.801	0.152

p values indicate differences between 4st week and 1st week. $p < 0.05$ was considered statistically significant. BUN, blood urea nitrogen; SCr, serum creatinine; eGFR, glomerular filtration rate; COVID-19, coronavirus disease 19; CKD, chronic kidney disease.

Notable points:

1. COVID19 was confirmed with THROAT swabs for RTPCR
2. AKI in adults defined as one of the following
    a. Increase in serum creatinine by ≥26 μmol/L (0.3 mg/dL) within 48 h, or an increase in SCr to >1.5 times baseline [the lowest value recorded] within the previous 7 days, or urine volume <0.5 mL/kg/h for >6 hrs

Risk-adapted Treatment Strategy For COVID-19 Patients.

PMID: 32229257Apr 2, 2020

Zheng, Changcheng; Wang, Jinquan; Guo, Hui; Lu, Zhaohui; Ma, Yan; Zhu, Yuyou; Xia, Daqing; Wang, Yinzhong; He, Hongliang; Zhou, Jian; Wang, Yong; Fei, Mingming; Yin, Yihong; Zheng, Mao; Xu, YehongInt J Infect Dis

BACKGROUND: There are no clear expert consensus or guidelines on how to treat 2019 coronavirus disease (COVID-19). The objective of this study is to investigate the short-term effect of risk-adapted treatment strategy on patients with COVID-19.

METHODS: We collected the medical records of 55 COVID-19 patients for analysis. We divided these patients into mild, moderate and severe groups, and risk-adapted treatment approaches were given according to the illness severity.

RESULTS: Twelve patients were in mild group and 22 were in moderate group (non-severe group, n=34), and 21 patients were in severe group. At the end of the first two weeks after admission, clinical manifestations had completely despeared in 31(91.2%)patients in non-severe group, and 18(85.7%) patients in severe group (p=0.85). Both groups had a satisfied chest CT imaging recovery, which includes 22(64.7%) patients in non-severe group and 12(57.1%) patients in severe group recovered at least 50% of the whole leisions in the first week, and 28(82.4%) and 16(76.2%) recovered at least 75% in the second week, respectively. There were no significant differences in SARS-CoV-2 RNA clearance between two group (p=0.92). There were also no significant differences in the levels of SARS-CoV-2-IgM and IgG antibody production between the two groups (p=0.13, 0.62).

There were 45 cases were discharged from the hospital, and no patients died at the time of this clinical analysis.

CONCLUSIONS: Risk-adapted treatment strategy was associated with significant clinical manifestations alleviation and clinical imaging recovery. **In severe COVID-19 patients, early and short-term use of low-dose methylprednisolone was beneficial and did not delay SARS-CoV-2 RNA clearance and influence IgG antibody production.**

Key points:

1. COVID19 severity was classified as
    a. Mild: Fever and mild respiratory symptoms with imagine showing no or mild pneumonia
    b. Moderate: Fever, cough, CT inidicating typical coronavirus pneumonia but with stable vital signs, SpO2 >93% without an oxygen requirement
    c. Severe: with at least 1 of the following; respiratory rate >30 breath/min at rest, O2 sat <93% without O2 requirement, PaO2/FiO2 < or = tp 300mmHg with total lesions or chest CT more than 30% or evidence of rapid progression to 50% in 72 hours.

Table 1 Patient's characteristics and clinical outcomes

Characteristics	Non-severe COVID-19	Severe COVID-19	*p*
Total (n)	34	21	
Respiratory rate, median (range)	20(18-26)	28(22-36)	0.015
Heart rate, median (range)	81(60-108)	88(54-140)	0.012
Oxygen saturation on admission, median (range)	97(94-99)	94(88-98)	0.045
Neutrophil count, median (range) ($\times 10^9$/L)	2.77(0.93-5.93)	3.46(0.56-9.29)	0.06
Lymphocyte count, median (range) ($\times 10^9$/L)	1.55(0.74-2.0)	1.09(0.57-2.18)	0.008
CD3-T cells, median (range) (%)	76.8(62.9-89.6)	70.5(39.5-86.8)	0.002
Aspartate aminotransferase, median (range) (U/L)	23(10-66)	40(16-346)	0.005
Total bilirubin, median (range) (mmol/L)	10.2(6.9-47.4)	13.4(7.4-35.7)	0.06
Lactate dehydrogenase, median (range) (U/L)	194(114-293)	247(143-437)	0.004
Creatine kinase, median (range) (U/L)	53(24-152)	74(32-2324)	0.01
Hypersensitive troponin I, median (range) (pg/mL)	1.6(0-9.4)	5.3(0.5-4428)	0.007
C-reactive protein, median (range) (mg/L)	6.14(0.08-103)	29.9(3.14-114)	＜0.001
Fibrinogen, median (range) (g/L)	3.4(2.4-5.7)	5.3(3.3-8.1)	＜0.001
Fibrin/Fibrinogen degradation products, median (range) (mg/L)	1.35(1-15.2)	2.9(1-18.2)	＜0.001
D-dimer, median (range) (mg/L)	0.24(0.2-2.9)	1.0(0.2-5.0)	＜0.001
Interleukin-6, median (range) (ng/L)	27.6(3.6-280)	64.3(3.8-439)	0.02

Can Bioactive Lipids Inactivate Coronavirus (COVID-19)?

PMID: 32229155Apr 2, 2020

Das, Undurti NArch Med Res

SARS-CoV-2, SARS and MERS are all enveloped viruses that can cause acute respiratory syndrome. Arachidonic acid (AA) and other unsaturated fatty acids (especially eicosapentaenoic acd, EPA and docosahexaenoic acid DHA) are known to inactivate enveloped viruses and inhibit proliferation of various microbial organisms. The pro-inflammatory metabolites of AA and EPA such as prostaglandins, leukotrienes and thromboxanes induce inflammation whereas lipoxins, resolvins, protectins and maresins derived from AA, EPA and DHA not only suppress inflammation but also enhance would healing and augment phagocytosis of macrophages and other immunocytes and decrease microbial load. In view of these actions, it is suggested that AA and other unsaturated fatty acids and their metabolites may serve as endogenous anti-viral compounds and their deficiency may render humans susceptible to SARS-CoV-2, SARS and MERS and other similar viruses' infections. Hence, oral or intravenous administration of AA and other unsaturated fatty acids may aid in enhancing resistance and recovery from SARS-CoV-2, SARS and MERS infections.