



# INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

## CURRENT INTERNATIONAL CRISES - COVID-19 A Review

**Anjali Sudha**

Email-sudhaanjali1985@gmail.com

STAREX UNIVERSITY

**Address:** NH-48, Binola, P.O.Bhorakalan,  
Gurugram, Haryana  
122413

**Dr. Neelam Dhankhar**

Email-reenadhankhar@gmail.com

STAREX UNIVERSITY

**Address:** NH-48, Binola, P.O.Bhorakalan,  
Gurugram, Haryana  
122413

### ABSTRACT

The extension of COVID-19 is now expanding globally almost 213 countries as per the data of World Health Organization (WHO) on 25 April 2020. There is brand new public health crises which is threatening the whole world as emergent condition and the spread of 2019 novel corona virus (2019-covid) or as severe acute respiratory syndrome corona virus 2 (SARS COV-2). This covid-2019 is currently in focus since the starting of 2020 year. According to the data available this virus was originated in bird and bats species that are believed to behave as its natural hosts.

This disease was transmitted through inhalation or when u comes in touch with an infected person's droplets. Its incubation duration is in between 2 days to 14 days with the usual symptoms for this disease are typically fever, cough, fatigue, breathlessness, sore throat. The disease remain mild in most the population; but in some (normally the elderly patients), it can cause serious consequences like pneumonia, multi organ disorder and acute respiratory misery syndrome (ARDS). Here lot many people remain asymptomatic disease for this. Now-a-days treatments which are being used are majorly supportive. Strict preventive measures are also being also followed includes domestic isolation of the suspected ones and people with mild symptoms and also strict disease spread control measures in hospitals like droplet precautions and avoiding touch with the diseased ones. This virus is spreading quicker than its last two ancestors that are, Middle East respiratory syndrome corona virus (MERS-CoV) and SARS-CoV, however its mortality rate is lower than both of them. The global effect of this virus is unpredictable till now.

**Keywords:** COVID-19, Corona outbreak, SARS, MERS, Virus

## INTRODUCTION:

This 2019 novel corona virus (2019-nCoV) or severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) as it has named so far, unexpectedly spreading from its birthplace that is Wuhan City of Hubei Province in China to the rest of the arena. Since last few years, corona viruses were associated with tremendous disease outbreaks in Middle East and East Asia. The intense Middle East respiration syndromes (MERS) and acute respiratory syndrome (SARS) commenced to emerge in 2012 and 2002, respectively. In present this corona virus was emerged in 2019 which may additionally impose a global threat, given the currently going on epidemic not only in China but has speeded over number of other territories (1). Worldwide Health employees are presently making efforts to take care of this outbreak caused by novel Corona virus (at the beginning it was named as 2019-nCoV) firstly diagnosed in Wuhan City of Hubei Province in China, on 12 December 2019. Again on 11 February 2020, WHO (World Health Organization) made introduced to the world, generation of new member of corona virus family as CoV and associated sickness to be as “COVID-19”.

First group of patients was discovered to be 109 people somewhere linked to Wuhan South China Seafood Market in the Wuhan (2). Corona viruses is related to large family group of relatives of zoonotic viruses that gives illness starting from common cold and fever to intense respiratory problems. Those viruses which can be easily transmitted from the animals to human species called as zoonotic viruses. There are number of corona viruses were discovered, infecting and circulating in animal population but did not infect human species. COVID-19 is maximum latest to make leap to human infection. Common symptoms for COVID-19 disease are quite similar to inclusive respiratory problem symptoms include and common cold like shortness for breath, fever, dry cough, and mild or severe breathing difficulties. In most of the instances, this contamination can result into pneumonia, kidney failure, severe acute respiratory syndrome which can further lead to death. The infection is transmitting from diseased persons to healthy ones via droplets, which usually happens during sneezing or coughing (3).

As per World Health Organization (WHO), such viral illnesses keep on emerging and constitute a serious issue to public fitness in recent twenty years, numerous viral epidemics which include. Most currently, Middle East respiratory syndrome corona virus (MERS-CoV) was firstly diagnosed in 2012 in Saudi Arabia (4).

Corona viruses are basically enveloped viruses with positive sense RNA with the diameter of 60 nm to 140 nm along with spike like outgrowths on the outer surface provides it a look like a crown, when it was observed with the help of electron microscope; therefore it was named as corona virus [5]. Four variety of corona that has already found in humans like HKU1, 229E, NL63 and OC43 and they all causes mild respiration diseases (6). The COVID-19 that has emerged as a severe threat not only for United States but for whole globe and which basically originated in China, speeded faster than it was expected. Because of its rapid spread and higher potential to infect large number of people this outbreak has been declared as a “worldwide health emergency” by WHO on January 31st, 2020. At present, we aren't able to successfully deal with COVID-19 due to the fact that neither approved specific antiviral drugs nor vaccines for treatment of human against CoV viruses has been invented (7-9). Very likely symptoms of COVID19 are headache fever, expectoration, cough, myalgia and dyspnea at the same time lesser common symptoms found were hemoptysis, shortness for breath and diarrhea (10). The updated data about the COVID-19 epidemic in China may additionally develop as severe epidemic or

maybe this virus can give serious loss to the world if timely actions will not taken with effective treatment.(11)

## History

Human corona viruses history of started from 1965 while Tyrrell and Bynoe<sup>1</sup> determined that there is different type of virus found which was named B814. It discovered in the human embryonic tracheal organ cultures which were found in respiratory tract of some adult who was surfing with common cold. (12) In late 1960s, Tyrrell who was working as leading scientist of a team, this group was working with different animal viruses including, infectious mouse hepatitis virus, transmissible gastroenteritis virus and bronchitis virus, they almost looked similar morphologically under electron microscopy (13-14). Such new cluster of viruses further named as corona virus (here corona depicts the crown-like look because of its surface projections) and become later on officially as an established new genus in the world of viruses. (15) Four other corona viruses like NL63, HKU1, OC43 and 229E had been found in humans, and typically causes respiratory disorders. Few incidences have been taken in notice where these viruses transmitted from animals to humans and resulted into some serious problems. First such instance came into notice in between 2002– 2003, while a new corona virus of this  $\beta$  genera and also with those originated in bats and carried forward to humans through some intermediate host like palm civet cats in China in the Guangdong province. This corona virus, exactly as SARS-CoV severe acute respiratory syndrome corona virus which affected almost 8422 of human beings in Hong Kong and China and finally brought about 916 deaths (calculated mortality rate was 11%) [16]. Then in 2012 almost a decade later, (MERS-CoV) Middle East breathing syndrome corona virus, which was also originated in bat, found only in Saudi Arabia region in dromedary camels like as intermediate host and finally affected 2494 humans and also triggered 858 deaths (fatality mortality 34%) [17].

## ORIGIN AND SPREAD OF COVID-19

At December 31 2019, the outbreak of COVID-19 was notified in China by WHO (World Health Organization). As a result on 1st January this sea food market of Wuhan has been closed by government. Then on 7th January that virus was also identified like a new virus as corona virus which was >95% similar to the gene structure of bat corona virus DNA and also > 70% homology

with SARS-CoV. Additionally Wuhan sea grocery store items were checked for Environmental samples for high quality, it has signified that the virus was originated from there [18]. On 11th January 2020 corona virus, first deadly case was identified. Chinese people large migration of Chinese people on the New Year alongside increased spread of this epidemic. More cases for corona were identified specially those people who were returning from china to international locations (Japan, South Korea, Thailand). It is now transmitted n to those healthcare people, were taking care for patients were taken in account on 20th Jan, 2020. As a result by 23rd of January, eleven million of people of Wuhan were put into strict lock down along with the restrictions of any access or exit from that place. Very Soon lock down was expended to various cities of the Hubei province. All the cases of COVID-19 which were in outdoor countries from China were supposed to get the infection by human-to-human transmission although they had no travelling history to china directly [19].

Till 05 March 2020 total 96,000 cases were identified globally (8000 alone in China) also 87 different international locations and 1 international conveyance were determined [20]. The current conditions say that there is a possibility of COVID-19 epidemic will grow in China additionally intensely if strict measures for prevention and control will not be taken timely (21). In India, only 3 cases were reported till 2nd march 2020, has additionally visible a surprising spurt in instances. By five/3/2020, 29 and by 5th march 2020 total 29 cases were there from which maximum cases were present in Jaipur, Agra, and Delhi. These 29 cases were not only Italian travelers but also those who have come into their direct or indirect contacts. One case was determined in India who was returned after travelling from Vienna and except this, exposed a massive variety of youngsters and faculty in a birthday celebration at in a city resort. These many of contacts of were quarantined to check the spread further. These numbers of sufferers were in somewhere underestimated because of limitations of proper checking and surveillance. Though SARS-CoV-2 was basically originated from bats, the intermediary animal through which transmitted this disease this to humans is unsure. For corona snakes and Pangolins are the contemporary suspects (21).

## **Coronavirus in Human**

Corona virus contamination in people is usually related to moderate to severe respiratory diseases which can be identified through symptoms excessive like cough, severe inflammation, fever, and internal organs disorder which will finally cause death (22). Immune response of a person is also important to manipulate and avoid Corona virus. While, weak immune system, will also contribute to disturbed immunopathology of a person and lead to imbalanced pulmonary gas exchange. Understanding the relation among innate immune systems for host and CoVs may increase our understanding about the process of how does this infection affects lung and also cause inflammation (23). Basically SARS is severe viral respiration sickness which was caused by unidentified animal corona virus which was originated in 'wet markets' in southern China thereafter it was carried away to a human host, from where it was further transferred among humans too (24). SARS epidemic was reported in year of 2002-03 has reached to 774 general of deaths (mortality rate 9.6%) (25). Then MERS was also a respiratory ailment that was firstly seen in Saudi Arabia in the year 2012. For MERS ailment fatality rate was around 35% near about (26).

Longest noted incubation time of 503 SARS-CoV-2 (COVID-19) is 14 days. For this reason, suspected people were quarantined up to 14 days 504 to majorly avoid the chances of spread (27) ill now Bats are being considered as corona virus important natural host in both of cases like MERS-CoV 520 and SARS-CoV infections, while likely intermediate host in SARS-CoV and for MERS-CoV 521 is Palm civet and Dromedary camel, respectively (28). For now Bats are being taken as an ancestral 522 hosts for each of the infection like MERS and SARS (103). Bats are also being considered as reservoir host for human species 523 for other varieties of corona viruses like HCoV-NL63 and HCoV-229E (29). In case of COVID-19, 524 two major possibilities are there for transmission number one ; both MERS and SARS can be easily transmitted via intermediate 525 hosts like once from bats (30). In case of SARS epidemic it has been shown that SARS-CoV was originated from 527 natural reservoir hosts, bats and then later on it jumped to an intermediate host, civet and adapted changes 528 inside the new host for receptor-binding domain (RBD) which increased its binding towards civet ACE2. Now this civet 529 adapted virus came into contact with humans and then transmitted among human species human to human transfer lead to an epidemic (29). Transmission can also take place 531 from reservoir host to the humans without any RBD adaptations. Bat corona virus this is 532

currently in many has recognized its exclusive feature like “poised” spike proteins which facilitate capability to infect without any need of adaptations or mutations (31). These findings are important in identifying the right opportunity about the interspecies transmission of SARS-CoV. Additionally SARS-like corona viruses have been identified in Chinese horseshoe bat (*Rhinolophus sinicus*) populations. In in vitro and also in vivo research it was tested that corona virus can be a serious threat and for re-emergence of SARS-CoV like diseases (31)

## Pathogenesis

The serious signs or symptoms for COVID-19 are associated with an increasing numbers of patients especially in the epidemic location which is China. At January 22, 2020, China National Health Commission declared 17 deaths and then on date January 25, 2020 this number reached directly to 56 deaths. The percentage of loss of life a number was 2.84% out of 2684 cases of COVID-19 on date Jan 25, 2020 and maximum death were observed from 48 to 89 years [32]. Those patients, suffered from COVID-19 were confirmed with ordinary respiratory findings but increased leukocyte numbers and also increased levels of plasma seasoned-inflammatory cytokines. One more COVID-19 case was found with five days of fever along with heavy respiratory sounds of lungs, cough, and increased temperature of 39.0°C. Later on patient's sputum has confirmed only by test procedures like real-time polymerase chain reaction results that showed COVID-19 infection [33]. Primary pathogenesis for COVID-19 infection was mistaken to be pneumonia as respiratory system disorder. Remarkably increased blood levels of cytokines were determined in patients, suffering with COVID-19 that comprises IL1RA, IL1- $\beta$ , IL7, IL10, IL9, IL8 basic FGF2, GCSF, IFN $\gamma$ , IP10, GMCSF, MIP1 $\alpha$ , MIP1 $\beta$ , MCP1, TNF $\alpha$ , PDGFB and VEGFA. Few cases that had been admitted to (ICU) intensive care unit they showed higher levels of pro-inflammatory cytokines comprises IL10, IL7, IL2, GCSF, MCP1, IP10, TNF $\alpha$  and MIP1 $\alpha$  which were main culprits for the severity of the disease [34].

## Transmission

Based at large variety of infected human beings, has been exposed to wet animal market in the Wuhan City wherein live animals are offered too, so there is a probability that is may be a origin

place for corona animal to human transfer. Further it was discovered that there were intermediate vendors or natural reservoir host from whom this infection would have spreader to the humans. Initial scientist has found out two species of the snakes that may be a responsible reservoir of COVID-19. Although till now, there is no strong evidence that corona virus resides except birds and mammals [35, 36]. After analysis of genomic sequences and comparison it was found that there is 88% similarity among COVID-19 and two bat-originated severe acute respiratory syndrome (SARS)-like corona viruses [37,38], It indicates that mammals are hyperlink between COVID-19 and human beings.

Number of reviews also have suggested that human to human transmission most possible way for this disease to get transferred [39,40]. Person-to-man or woman transmission occurs usually either by direct touch or may be through droplets spread via sneezing or coughing from an already infected individual. There was no evidence that there's transmission from mom to child in a women in her third trimester who were showed to be infected with corona virus. But, all those pregnant mothers who have been through cesarean sections only, so it is hard to say whether transmission can occur with vaginal birth or not. First step of the viral infection is binding of receptor expressed via host cells by fusion with cell membrane. primary target for the virus are Lung epithelial cells SARS-CoV human-to-human transmissions takes place via the binding among receptor-mobile receptor and binding domain of virus spikes which were identified as the angiotensin-changing enzyme 2 (ACE2) receptors [41,42].

### **Prevention, Control and Management:**

The first step is to assure quarantine (discussed later) to save you from transmission from different contacts, also patients and healthcare people too. The standard concepts were like, taking required nutrients and remaining hydrated and controlling cough and fever. Suggestions as per Chinese is low dose corticosteroids within brief time of period remedy in COVID-19 ARDS [43,44]. Detailed suggestions and special care tips to be taken has already been published by WHO for COVID-19 [45]. Till now, there is no authorized treatment available for COVID-19. When it is compared with China's condition in 2002, when it suffering with a SARS outbreak, there were more of political openness while reporting for COVID-19 outbreak. They also have made gene sequencing of COVID-19 and did share it globally (46). Chances of COVID-19 to



cause nosocomial infections are high and for this reason manipulate and preventive measures are mandatory to be taken(47). Following the epidemic, a temporary kind of ban was imposed on wildlife exchange also keeping in mind that possibly they can transfer SARS-CoV-2/COVID19 (48). To control the spillover of corona virus it is necessary to take bold steps like controlling the exchange of animals between countries (49).

Human-to-human transmission of SARS-CoV-2 not only takes place by direct contact but also by droplets. Because of this, the first line health workers need to take extra preventive measures like PPE (personal protective equipment) for infection control (50). Their mental fitness is need to be taken care of delicately in COVID-19 as such kind of environment can seriously affect their concentration, selection-making capacity and interest. Therefore, for better management of COVID-19 outbreak, important steps are being taken for preference of mental fitness of the clinical workers (51) As the animals present in wet market can be a an easy intermediate host for SARS-CoV-2. Government has taken mandatory steps for prevention measures and emergency control. They already have established a hospital for the treatment of suspected and infected ones and many more such steps are being taken to decrease the possibilities of continuous spread through infected population (52). In addition to isolation and quarantine of infected ones effective techniques are also being adapted for better testing for SARS-CoV 2/COVID-19. To decrease the probabilities of further spread of this epidemic strict preventive and control measures has been adapted. (53) In Chinese cities, major movement activities are being control because of COVID-19 epidemic (54). Therefore, efficient health workers can play a major role here. Medical doctor who warned first about this virus has died unfortunately. It is very important to give good protection to the healthcare workers if uninterrupted services are expected from them and continuously effective treatment is required [55, 56]

### **Virus Isolation**

For virus isolation Special-pathogen-free human airway epithelial (HAE) cells were used. Briefly, from the patients broncho-alveolar lavage fluids or throat swabs were inoculated into the HAE cells through the apical surfaces. In an air–liquid interface HAE cells were maintained and incubated at 37°C. For cytopathic effects, the cells were monitored daily by light microscopy

and the cell supernatants were collected for use in quantitative RT-PCR assays. Apical samples were collected after three passages, for sequencing. [57]

### **Therapy so far:**

#### **Chloroquine and Hydroxychloroquine :**

Two medicines that have been used for many decades to treat malaria and autoimmune diseases such as rheumatoid arthritis and lupus are hydroxychloroquine and chloroquine[58]. Coronaviruses are single-stranded RNA viruses that encode four enzymes that are important to the cycle of viral life. Via an interaction of a viral spike glycoprotein and a receptor-ACE2 for SARS-CoV-1 and SARS-CoV-2 they invade mammalian cells. These drugs function by inhibiting viral ACE-2 glycosylation or quinone reductase inhibition, reducing viral sialic acid synthesis. [59-60] To the FDA for emergency purposes only. For its antiviral ability against SARS-CoV-induced cytopathicity in Vero E6 cell culture, chloroquine phosphate. Results show that chloroquine IC50 for antiviral activity (8.8 +/- 1.2 microM) was significantly lower than its cytostatic activity; CC50 (261.3 +/- 14.5 microM) was significantly lower, resulting in a selectivity index of 30. In the prevention and treatment of SARS-CoV infections, chloroquine, an old antimalarial medication, may be considered for immediate use. [61] It is only authorised for emergency purposes by the FDA.

#### **Drugs in clinical trials are:**

As per report of WHO (excess on 5 April), Treatment option under study

- a) Remdesivir was previously tested as an Ebola treatment.
- b) For treatment of HIV Lopinavir /Ritonavir is a licensed.
- c) To treat multiple sclerosis Interferon beta-1a is used.
- d) To treat malaria and rheumatology conditions respectively, Chloroquine and hydroxychloroquine are very closely related and used.

**Chloroquine:** Used as a preventative medicine for COVID-19 treatment. Clinical condition is 10000 participants in a prophylaxis study for COVID-19. [62]

**Hydroxychloroquine:** The drug is used as mono-therapy for treatment for hospitalized COVID-19 patients. [63]

**Combination of Hydroxychloroquine and azithromycin:** For this open-label, randomized Controlled trial of Hydroxychloroquine and Azytromicyn will conducted for COVID-19 patients which are not in critical condition and are hospitalized due to infection. In a recent trial, for COVID-19 treatment treated with hydroxychloroquine in combination with the macrolide antibiotic azithromycin were virologically cured comparing with 57.1% in patients treated with hydroxychloroquine alone, and 12.5% in the control group [63]

**Combination of Hydroxychloroquine Sulfate and azithromycin:** This is exploratory, open label, multi-center study for the evaluation of efficacy of drug to treat moderate to severe COVID-19 pneumonia Caused by SARS-CoV-2 Virus [64]

**Remdesivir:** The study is evaluate the safety and efficacy drug for hospitalized COVID-19 adults' diagnosed positive. This is a multicenter trial across 75 sites globally. Study started on February 21, 2020. [65]

**Camostat Mesilate :** This is Serine protease inhibitor, blocks TMPRSS-2 mediated cell entry of SARS-CoV-2. This is Randomized, Quadruple means consists of Participant, Care Provider, Investigator and Outcomes Assessor and Placebo-controlled study. Study firstly submitted on March 23, 2020. Clinical status as evaluate by the 7-point ordinal scale at day 7, 14 and 30, which means unsightly, no limitations on activities.[66]

**Ivermectine:** A recent study found the promising *in-vitro* activity of Ivermectine (FDA-approved anti-parasitic) with the  $IC_{50} = 2\mu M$  for COVID- 19 and the duration of cell load inhibition was found 48 hr [67].

## Conclusion:

WHO declared a health emergency in the world from the deadly virus COVID-19, which came up with an extra ordinary challenge for the entire human race. He current approaches lead us to

some of the previously approved FDA drugs, which are showing results against COVID-19. It will be very crucial for upcoming days related to the clinical studies. The need of COVID-19 drug is the most urgent in the current scenario. Hope this in-vitro and initial phase study of the drug will be an asset for the human kind.

**Funding - NA**

**Conflicts of interest- None**

**Acknowledgment:**

Thanks, HIMT college of pharmacy for providing space/

**Abbreviations:**

**WHO:** World Health Organization

**FDA:** Food and drug administration

**COVID-19:** Coronavirus disease 2019

**SARS:** Serious acute respiratory syndrome

**HCV:** Human coronavirus

**ACE2:** Angiotensin-converting enzyme 2

**CRFK-** Crandell-Reese Feline kidney cells

**FIPV-** Feline infectious peritonitis virus

**CHIKV-** Chikungunya virus

**REFERENCES**

1. Rodriguez-Morales AJ, Bonilla-Aldana DK, Balbin-Ramon GJ, Rabaan AA, Sah R, Paniz-Mondolfi A, Pagliano P, Esposito S. 2020. History is repeating itself: Probable zoonotic spillover as the cause of the 2019 novel Coronavirus Epidemic. *Infez Med* 28(1):3-5
2. Gralinski LE, Menachery VD. 2020. Return of the Coronavirus: 2019-nCoV. *Viruses* 12(2):E135. doi: 10.3390/v12020135.
3. <https://www.labmanager.com/lab-health-and-safety/covid-19-a-history-of-coronavirus-2021>
4. Perlman S, Netland J. Coronaviruses post-SARS: update on replication and pathogenesis. *Nat. Rev. Microbiol.* 2009 Jun;7(6):439-50.

5. Richman DD, Whitley RJ, Hayden FG. *Clinical Virology*, 4th ed. Washington: ASM Press; 2016.
6. Chan-Yeung M, Xu RH. SARS: epidemiology. *Respirology*. 2003;8:S9–14.
7. Lu H. 2020. Drug treatment options for the 2019-new coronavirus (2019-nCoV). *Biosci Trends* 10.5582/bst.2020.01020. doi: 10.5582/bst.2020.01020.
8. Sheahan TP, Sims AC, Leist SR, Schäfer A, Won J, Brown AJ, Montgomery SA, Hogg A, Babusis D, Clarke MO, Spahn JE, Bauer L, Sellers S, Porter D, Feng JY, Cihlar T, Jordan R, Denison MR, Baric RS. 2020. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. *Nat 1335 Commun* 11(1):222. doi: 10.1038/s41467-019-13940-6.
9. Pillaiyar T, Meenakshisundaram S, Manickam M. 2020. Recent discovery and 1337 development of inhibitors targeting coronaviruses. *Drug Discov Today* S1359-6446(20)30041-6. doi: 10.1016/j.drudis.2020.01.015.
10. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, Li SB, Wang HY, Zhang S, Gao 1353 HN, Sheng JF, Cai HL, Qiu YQ, Li LJ. 2020a. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ* 368:m606. doi: 10.1136/bmj.m606
11. Chen J. 2020. Pathogenicity and transmissibility of 2019-nCoV-A quick overview and 1357 comparison with other emerging viruses. *Microbes Infect* S1286-4579(20)30026-5. 1358 doi:10.1016/j.micinf.2020.01.004.
12. Tyrrell DA, Bynoe ML. Cultivation of viruses from a high proportion of patients with colds. *Lancet*. 1966;1:76–77.
13. McIntosh K, Becker WB, Chanock RM. Growth in suckling-mouse brain of “IBV-like” viruses from patients with upper respiratory tract disease. *Proc Natl Acad Sci USA*. 1967;58:2268–2273.
14. Witte KH, Tajima M, Easterday BC. Morphologic characteristics and nucleic acid type of transmissible gastroenteritis virus of pigs. *Arch Gesamte Virusforsch*. 1968;23:53–70.
15. Tyrrell DA, Almeida JD, Cunningham CH, et al. Coronaviridae. *Intervirology*. 1975;5:76–82.
16. Chan-Yeung M, Xu RH. SARS: epidemiology. *Respirology*. 2003;8:S9–14.

17. Middle East Respiratory Syndrome Coronavirus. Available at: <https://www.who.int/emergencies/mers-cov/en/>. Accessed 16 Feb 2020
18. Xinhua. China's CDC detects a large number of new coronaviruses in the South China seafood market in Wuhan. Available at: [https://www.xinhuanet.com/2020-01/27/c\\_1125504355.htm](https://www.xinhuanet.com/2020-01/27/c_1125504355.htm). Accessed 20 Feb 2020
19. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *N Engl J Med*. 2020. <https://doi.org/10.1056/NEJMc2001468>.
20. Coronavirus Outbreak. Available at: <https://www.worldometers.info/coronavirus/>. Accessed 23 Feb 2020.
21. Chen J. 2020. Pathogenicity and transmissibility of 2019-nCoV-A quick overview and comparison with other emerging viruses. *Microbes Infect* S1286-4579(20)30026-5. doi:10.1016/j.micinf.2020.01.004.
22. Kritas SK, Ronconi G, Caraffa A, Gallenga CE, Ross R, Conti P. 2020. Mast cells contribute to coronavirus-induced inflammation: new anti-inflammatory strategy. *J Biol Regul Homeost Agents* 34(1):10.23812/20-Editorial-Kritas. doi: 10.23812/20-1613 Editorial-Kritas.
23. Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, Pan P, Wang W, Hu D, Liu X, Zhang Q, Wu J. 2020a. Coronavirus infections and immune responses. *J Med Virol* 10.1002/jmv.25685. 1388 doi: 10.1002/jmv.25685.
24. Peiris JS, Guan Y, Yuen KY. 2004. Severe acute respiratory syndrome. *Nat Med* 10(12 Suppl): S88-97. doi: 10.1038/nm1143.
25. WHO. 2003. World Health Organization. Consensus document on the epidemiology of severe acute respiratory syndrome (SARS). Available online: <https://www.who.int/csr/sars/en/WHOconsensus.pdf> (accessed on 29 January 2020).
26. WHO. 2019. World Health Organization. Middle East respiratory syndrome coronavirus (MERS-CoV). Available online: [https://www.who.int/en/news-room/fact-sheets/detail/middle-east-respiratory-syndromecoronavirus-\(mers-cov\)](https://www.who.int/en/news-room/fact-sheets/detail/middle-east-respiratory-syndromecoronavirus-(mers-cov)) (accessed on 29 January 2020).
27. Jiang X, Rayner S, Luo MH. 2020a. Does SARS-CoV-2 has a longer incubation period 1634 than SARS and MERS? *J Med Virol* 10.1002/jmv.25708. doi: 10.1002/jmv.25708.

28. Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, Zhu H, Zhao W, Han Y, Qin C. 2019. 1645 From SARS to MERS, Thrusting Coronaviruses into the spotlight. *Viruses* 11(1):59. doi: 1646 10.3390/v11010059.
29. Graham RL, Donaldson EF, Baric RS. 2013. A decade after SARS: strategies for 1650 controlling emerging coronaviruses. *Nat Rev Microbiol* 11(12):836-848. doi: 1651 10.1038/nrmicro3143.
30. Perlman S. 2020. Another decade, another coronavirus *N Engl J Med* 1648 10.1056/NEJMe2001126. doi:10.1056/NEJMe2001126.
31. Menachery VD, Yount BL Jr, Debbink K, Agnihothram S, Gralinski LE, Plante JA, 1653 Graham RL, Scobey T, Ge XY, Donaldson EF, Randell SH, Lanzavecchia A, Marasco 1654 WA, Shi ZL, Baric RS. 2015. A SARS-like cluster of circulating bat coronaviruses 1655 shows potential for human emergence. *Nat Med* 21(12):1508-1513. doi: 1656 10.1038/nm.3985.
32. W. Wang, J. Tang, F. Wei Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. *J. Med. Virol.*, 92 (4) (2020), pp. 441-447, 10.1002/jmv.25689
33. J. Lei, J. Li, X. Li, X. Qi CT imaging of the 2019 novel coronavirus (2019-nCoV) pneumonia *Radiology* (2020), p. 200236, 10.1148/radiol.2020200236
34. C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China *Lancet*, 395 (10223) (2020), pp. 497-50
35. M. Bassetti, A. Vena, D. Roberto Giacobbe The Novel Chinese Coronavirus (2019-nCoV) Infections: challenges for fighting the storm *Eur. J. Clin. Invest.* (2020), Article e13209, 10.1111/eci.13209
36. W. Ji, W. Wang, X. Zhao, J. Zai, X. Li Homologous recombination within the spike glycoprotein of the newly identified coronavirus may boost cross-species transmission from snake to human *J. Med. Virol.*, 92 (4) (2020), pp. 433-440, 10.1002/jmv.25682
37. R. Lu, X. Zhao, J. Li, P. Niu, B. Yang, H. Wu, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding *Lancet*, 395 (10224) (2020), pp. 565-574, 10.1016/S0140-6736(20)30251-8

38. Y. Wan, J. Shang, R. Graham, R.S. Baric, F. Li Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS J. Virol. (2020), 10.1128/JVI.00127-20
39. W.G. Carlos, C.S. Dela Cruz, B. Cao, S. Pasnick, S. Jamil Novel wuhan (2019-nCoV) coronavirus
40. P. Wu, X. Hao, E.H.Y. Lau, J.Y. Wong, K.S.M. Leung, J.T. Wu, et al. Real-time tentative assessment of the epidemiological characteristics of novel coronavirus infections in Wuhan, China, as at 22 January 2020 Euro Surveill., 25 (2020)
41. Y. Wan, J. Shang, R. Graham, R.S. Baric, F. Li Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS J. Virol. (2020), 10.1128/JVI.00127-20
42. J.A. Jaimes, J.K. Millet, A.E. Stout, N.M. Andre, G.R. Whittaker A tale of two viruses: the distinct spike glycoproteins of feline coronaviruses
43. Guan Y, Zheng BJ, He YQ, Liu XL, Zhuang ZX, Cheung CL, Luo SW, Li PH, Zhang LJ, Guan YJ, Butt KM, Wong KL, Chan KW, Lim W, Shortridge KF, Yuen KY, Peiris JS, Poon LL. 2003. Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China. Science 302(5643):276-278. doi: 10.1126/science.1087139.
44. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Lancet. 2020;395:473–5.
45. Zhao JP, Hu Y, Du RH, et al. Expert consensus on the use of corticosteroid in patients with 2019-nCoV pneumonia. Zhonghua Jie He He Hu Xi Za Zhi. 2020;43:E007
46. WHO. Clinical management of severe acute respiratory infection when novel coronavirus [nCoV] infection is suspected. Available at: [https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\[ncov\]-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-[ncov]-infection-is-suspected). Accessed 9 Feb 2020
47. Nkengasong J. 2020. China's response to a novel coronavirus stands in stark contrast to 2002 the 2002 SARS outbreak response. Nat Med 10.1038/s41591-020-0771-1. doi: 10.1038/s41591-020-0771-1.



48. Cheng VCC, Wong SC, To KKW, Ho PL, Yuen KY. 2020. Preparedness and proactive  
1531 infection control measures against the emerging Wuhan coronavirus pneumonia in  
China 1532 *J Hosp Infect* S0195-6701(20)30034-7. doi:10.1016/j.jhin.2020.01.010.
49. Wang N, Li SY, Yang XL, Huang HM, Zhang YJ, Guo H, Luo CM, Miller M, Zhu G,  
1811 Chmura AA, Hagan E, Zhou JH, Zhang YZ, Wang LF, Daszak P, Shi ZL. 2018b.  
1812 Serological evidence of bat SARS-related Coronavirus infection in humans, China.  
Virol 1813 *Sin* 33(1):104-107. doi: 10.1007/s12250-018-0012-7
50. Rodriguez-Morales AJ, Bonilla-Aldana DK, Balbin-Ramon GJ, Rabaan AA, Sah R, 1312  
Paniz-Mondolfi A, Pagliano P, Esposito S. 2020. History is repeating itself: Probable 1313  
zoonotic spillover as the cause of the 2019 novel Coronavirus Epidemic. *Infez Med* 1314  
28(1):3-5.
51. Wu YC, Chen CS, Chan YJ. 2020b. Overview of the 2019 novel Coronavirus (2019- 1672  
nCoV): The pathogen of Severe Specific Contagious Pneumonia (SSCP). *J Chin Med*  
1673 Assoc 10.1097/JCMA.0000000000000270. doi:  
10.1097/JCMA.0000000000000270
52. Kang L, Li Y, Hu S, Chen M, Yang C, Yang BX, Wang Y, Hu J, Lai J, Ma X, Chen J,  
2096 Guan L, Wang G, Ma H, Liu Z. 2020. The mental health of medical workers in  
Wuhan, 2097 China dealing with the 2019 novel coronavirus. *Lancet Psychiatry* S2215-  
2098 0366(20)30047-X. doi: 10.1016/S2215-0366(20)30047-X.
53. Guan W, Xian J. 2020. The progress of 2019 Novel Coronavirus (2019-nCoV) event in  
2100 China. *J Med Virol* 10.1002/jmv.25705. doi: 10.1002/jmv.25705.
54. Tang B, Wang X, Li Q, Bragazzi NL, Tang S, Xiao Y, Wu J. 2020. Estimation of the 2093  
transmission risk of the 2019-nCoV and its implication for public health interventions. *J*  
2094 *Clin Med* 9(2):E462. doi: 10.3390/jcm9020462.
55. Wu JT, Leung K, Leung GM. 2020c. Nowcasting and forecasting the potential domestic  
2102 and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a  
2103 modelling study. *Lancet* S0140-6736(20)30260-9. doi: 10.1016/S0140-  
6736(20)30260-9
56. Li J, Li J, Xie X, et al. Game consumption and the 2019 novel coronavirus. *Lancet Infect*  
Dis. 2020. [https://doi.org/10.1016/S1473-3099\(20\)30063-3](https://doi.org/10.1016/S1473-3099(20)30063-3)

57. Y.H. Jin, L. Cai, Z.S. Cheng, H. Cheng, T. Deng, Y.P. Fan, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version) *Mil. Med. Res.*, 7 (2020), p. 4
58. W. Wang, J. Tang, F. Wei Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China *J. Med. Virol.*, 92 (4) (2020), pp. 441-447, 10.1002/jmv.25689
59. Q. Li, X. Guan, P. Wu, X. Wang, L. Zhou, Y. Tong, et al. Early transmission dynamics in wuhan, China, of novel coronavirus-infected pneumonia *N. Engl. J. Med.* (2020), 10.1056/NEJMoa2001316
60. A. Assiri, J.A. Al-Tawfiq, A.A. Al-Rabeeh, F.A. Al-Rabiah, S. Al-Hajjar, A. Al-Barrak, et al. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study *Lancet Infect. Dis.*, 13 (2013), pp. 752-761
61. N. Lee, D. Hui, A. Wu, P. Chan, P. Cameron, G.M. Joynt, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong *N. Engl. J. Med.*, 348 (2003), pp. 1986-1994
62. <https://www.goodrx.com/blog/coronavirus-treatments-on-the-way/>
63. <https://www.cebm.net/covid-19/registered-trials-and-analysis/>
64. Ali Rismanbaf, Potential Treatments for COVID-19; a Narrative Literature Review, *Arch Acad Emerg Med.* 2020; 8(1): e29.
65. Keyaerts E, Vijgen L, Maes P, Neyts J, Van Ranst M., In vitro inhibition of severe acute respiratory syndrome coronavirus by chloroquine, *Biochem Biophys Res Commun.* 2004, 323(1):264-8.
66. Caly, L., Druce, J.D., Catton, M.G., Jans, D.A., Wagstaff, K.M., The FDA-approved Drug Ivermectin inhibits the replication of SARS-CoV-2 in vitro, *Antiviral Research.*
67. <https://www.drugtargetreview.com/news/59414/ivermectin-shows-activity-against-covid-19-in-cell-cultures/>