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SARS-CoV-2 - Understanding for the Preparation of Forthcoming Corona Virus Outbursts

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Abstract

A new major epidemic foci of corona virus disease 2019 known as COVID-19, previously known as 2019-nCoV have been identified and rapidly expanding throughout the world without traceable origin since early 2020. The disease has drastically increased and the affected number of countries, states or territories reporting infection to WHO was more than 200[1]. The 2019 novel corona virus disease outbreak was instigated from Wuhan, Hubei province, China at late December 2019 and affirmed as a public health threat emerging of International anxiety on 30th January 2020 by WHO[2]. International Committee on Taxonomy of Viruses (ICTV) declared "Severe Acute Respiratory Syndrome Corona Virus (SARS-CoV2)" as the name of novel corona virus, because their genetically similarities with SARS outbreak in 2003. The present review focuses on morphological, genetical characterization of SARS – CoV – 2 as well as the clinical traits and clinical therapies for COVID – 19 endemic up to date. The novel coronavirus emergence awaken the echoes of SARS-CoV pandemic in past decades. Yet, with having best technological advance, the exact medication is still a question. It might be a great lesson to the world to equip to deal with most recent emergent viruses in future. The current work will give a deep understanding of CoV -2 to researcher for the further studies.

Keywords: COVID – 19; SARS CoV – 2; Etiology; Epidemiology; Clinical traits and Therapy.

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1. ORIGION AND EMERGENCE

Corona virus (CoV) is one of the chief pathogens which mainly aims respiratory system and liver of humans. The outbreaks of corona virus associated with severe acute respiratory syndrome was reported as

SARS-CoV in 2003 and Middle East respiratory syndrome coronavirus (MERS-CoV in 2009, which have been previously categorized as mediators that are of boundless public health risk.

SARS-CoV-2 is likely to be corona virus of bat origin exhibiting 96.2% full genome identify with a clad 2b beta-CoV from *Rhinolophus affinis* bats in Yunnan, China. Except SARS-CoV, all the other CoVs of clad 2b CoVs have been reported in bats. So far more than 500 CoVs have been identified in bats while more than 5,000 of unknown bat CoV diversity yet to be estimated.

The third zoonotic human SARS-CoV-2 was epidemiologically connected to a sea food and wet animal wholesale market in China[3,4]. The WHO stated that environmental samples taken from the marketplace have comeback positive for the novel corona virus, however no specific animal association has been known[5]. Most up – to – date work has been verified that many CoVs are capable of infecting human cells without a necessity of intermediary adaptation[6,7]. Corona virus of the century began in December-2019 with a group of patients with the symptoms comparable to SARS-CoV and MERS-CoV infections, patients showed signs of viral pneumonia in China[8]. During the middle of January-2020, the outburst was further extended to throughout China including Beijing, Shanghai, Shenzhen as well as another spread case to South Korea and later has expanded to outside countries[9].

2. ETHIOLOGY

The CoVs belongs to the family Coronaviridae with four genera named alpha CoV, beta CoV, delta CoV and gamma CoV[10,11]. The genomic characterization studies shows bats and rodents are the gene sources of alpha CoVs and beta CoVs while avian species for delta CoVs and gamma CoVs. Until now, a total of seven CoVs capable of infecting human have been identified. They are HCoV-OC43, HCoV-HKU1, SARS-CoV-229E, HCoV-NL63, MERS -CoV, SARS-CoV and SARS-CoV-2[12]. They cause common cold and self- limiting upper respiratory infection to epidemic with variable clinical severity featuring respiratory and extra respiratory manifestation. The SARS-CoV-2 belongs to beta CoVs category[13,14]. The novel corona virus has diverse epidemiological characteristics, making it more contagious than SARS-CoV and MERS-CoV[15].

3. SARS- CoV- 2

Corona viruses are a huge family of viruses that are common in people and specific animal including camels, cattle, cats and bats. The name corona is derived from a Latin word "*Coronam*" means crown. It has a round or eliptic and often pleomorphic form with a diameter of approximately 60-140 nm. The CoVs are positive stranded RNA of around 30 kb in length with crown morphology by the presence of glycoprotein spike on envelop (Fig. 1). The spike glycoprotein is made up of subunits S1 and S2, guiding the link to host receptor.

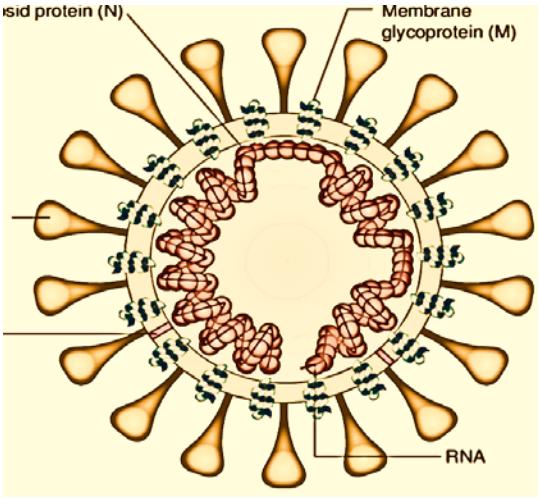

Fig. 1. Structure of SARS-CoV-2

Wu et al.[16] isolated whole genome of Wuhan Hu-1 corona virus (WHCV) along with a strain of SARS-CoV-2 of 29.9 kb from a COVID-19 pneumonia patient, while the genome size of SARS-CoV and MERS-CoV is 27.9 kb and 30.1 kb[17] and this viral genome consist variable number of open reading frames (ORFs)[18]. About 3/4 portion of viral RNA is responsible for the translation of polyproteins pp1a and pp1ab along with 16-non-structural proteins, accessory and structural proteins[19]. The remaining genome encodes for essential structural proteins; spike glycoproteins, envelop protein, matrix protein and nucleocapsid protein and numerous accessory proteins which involves with host instinctive immune reaction.

Both WHCV and SARS-CoV are genetically and phylogenetically seems to be similar[16]. The genomic study of SARS-CoV and MERS-CoV reveals, similarity of SARS-CoV with SARS-like bat CoVs[20] (Table 1). Angeletti et al.[21] reported that, the mutation at some non-structural proteins plays an important part in contagious ability of SARS-CoV-2. The study of genotype of COVID-19 patients from different provinces of china found that, SARS-CoV-2 had been mutated[22].

Table 1. Comparative analyses of SARS CoV – 2, SARS - CoV and MERS – CoV.

Characteristics	**SARS-CoV-2**	**SARS-CoV**	**MERS-CoV**
Estimated R_0	2.68	2-5	>1
Host	Bats – natural host pangolins- Intermediate hosts Humans -terminal hosts	Chinese horseshoe bats - natural hosts Masked palm civets - intermediate hosts, Humans - terminal hosts	Bats _ natural hosts Dromedary camels - intermediate hosts Humans -terminal hosts
Mode of Transmission	Human-to-human: physical contact, aerosol droplets, zoonotic transmission.	Human-to-human: physical contact, aerosol droplets, zoonotic transmission. Droplets, opportunistic airborne transmission, fecal-oral transmission.	Respiratory transmission, aerosol transmission zoonotic transmission, nosocomial transmission, limited human-to-human transmission
Incubation period	6.4 days (range: 0-24 days)	4.6 days	5.2 days

4. EPIDEMIOLOGY

The data provided by WHO Health emergency dashboard as on June 18, 2020; 06:00 (ET) confirmed 8,362,238 cases throughout the world since the beginning of the epidemic and 4,48,504 cases have been reported fatal (Fig. 2). China, the origin of current COVID-19 outbreaks confirmed 89,233 cases clinically and, in the laboratory, and reported deaths so far. Apart from china, there are cases were confirmed from 204 countries around the world[23].

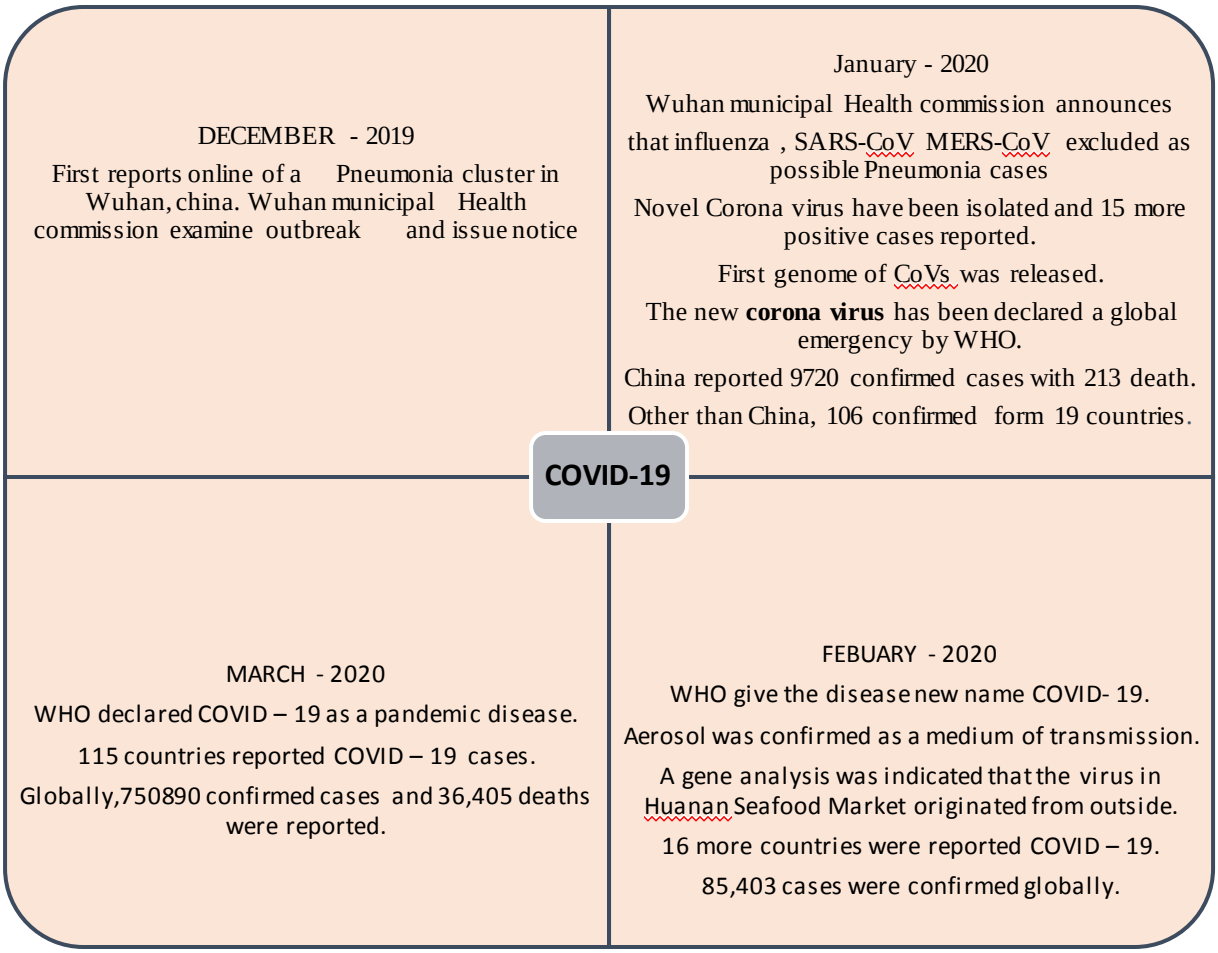

Fig 2. Timeline of the key SARS – CoV – 2, 2019 – 20 Corona virus pandemic events.

5. TRANSMISSION AND PATHOGENESIS

The COVs have become the major pathogens of emerging respiratory disease outbreak because it can cross species barriers and causes illness from clod mild to severe MERS and SARS[24]. The possibility of transmission of CoVs like other respiratory pathogens is believed to occur through respiratory droplets from coughing and sneezing[25,26].

Angiotensin-converting enzyme 2 (ACE-2), the cell receptor of SARS-CoV observed in the lower respiratory tract of humans is responsible for the regulation of both cross-species and transmission between humans [27-30]. The SARS-CoV-2 is also use similar cellular entry receptor like SARS-CoV [31, 32]. The glycoproteins spikes determine the virus-host range and cellular tropism with the key functional domain : receptor binding domain (RBD) and also arbitrates virus-cell membrane fusion [33,34]. Once the membrane fusion takes place, the viral genomic RNA is unconfined in to the cytoplasm and the uncoated RNA translates two polyproteins [35], which encodes non-structural proteins and replicase-transcriptase complex [36]. Further RTC synthesis sub-genomic RNAs [37] encode accessory and structural proteins and then form viral particle bud and start being replicated [38].

6. CLINICAL CHARACTERISTICS

COVID-19 is believed to be spread by the respiratory tracts of human being by droplet, respiratory secretion and even direct contact. The occurrence of SARS-CoV-2 in fecal swabs of severe pneumonia patient and blood indicates the multiple routs of transmission [39]. Abundance of ACE 2 proteins of SARS-CoV-2 in alveolar epithelial cells of lungs and enterocytes of small intestine, clarify the routes of infection and disease

manifestation [40]. According to the epidemiological study of SARS-CoV-2, the incubation period is 1- 14 days, while active during latency period. Guan et al. [41] reported that 47 years was the median age of corona infection and profound in female patients [42]. The most common symptoms were fever and cough at the beginning and later cause pneumonia, ARDS, RNAaemia, severe cardiac damage and secondary infections. At the critical condition, respiratory failure, multiple organ failure and even deaths may occur [43,44].

7. DIAGNOSTIC CRITERIA

The golden clinical diagnosis method is the nucleic acid detection of samples from nasal, throat (or) other respiratory swabs by real time PCR and further confirmed by next-generation sequencing. The ELISA test [45,46] is based on antibody with engineered SARS-CoV-2 outer envelope spike protein to stabilized form and isolated RBD, epitope for antibody generation. While CRISPR base detection test can be done with viral nucleic acid [47]. The updated computed tomography (CT) scoring measures that deliberates lobe involvement, as well as changes in CT findings, could quantitatively and exactly evaluate the advancement of corona virus disease [48,49].

8. CLINICAL SYMPTOMS

The symptoms of COVID-19 infections start to seem after an incubation period of 5 days[50]. While the infection from symptoms to death may range from 6 to 41 days with a median of 14 days [51] and it depends on the age and physical conditions of patients. The most common symptoms of COVID-19 includes cough, fever, fatigue at first, later sputum production, headache, haemoptysis, diarrhoea, dyspnoea and lymphopenia [52, 53, 54, 55] (Table 2).

Table 2. Systematic and Respiratory disorders due to COVID – 19 infection.

Systemic Disorders	Respiratory Disorders
Fever, Cough, Fatigue	Rhinorrhoea
Sputum production, Headache	Sneezing, Sore throat
Haemopysis	Pneumonia
Acute cardiac injury	Ground – glass opacities
Hypoxemia	RNAaemia, Acute Respiratory
Dyspnea, Lymphopenia	Distress syndrome.
Diarrhea	

There are resemblances were found in the symptoms between COVID-19 and earlier beta corona virus infectious includes fever, dry cough, dyspnea and bilateral ground-glass opacities on chest CT scans [56]. However certain unique clinical features like upper respiratory tract symptoms like rhinorrhea, sneezing, sore throat and dyspnea with hypoxemia among COVID-19 patients [57-62]. The disease tends to progress fast among the elderly people and showed a higher death risk [63, 64].

9. THERPEUTIC/TREATMENT OPTIONS

Host immune response and immunopathology

The immune response is more important for the resolution and control of CoVs infections among the patients. Meantime it also can end up in immunopathogenesis, related to the immune reactions out of management [19]. The virus particle primarily invades the respiratory mucosa and further infect other cells. The virus cell communications produce a varied set of immune mediators counter to the pathogenic virus [65] and later it elicits a series of immune response and cytokine production in the body, which may be allied with the serious condition of COVID-19 patients.

Treatments of COVID-19

The person-to-person spread of COVID-19 infection has headed to the isolation of patients that were directed a diversity of treatments. Due to the absence of exact antiviral drugs or vaccine against COVID-19, a

wide range of antiviral drugs like nucleoside analogous, HIV-protease inhibitors were favored to diminish virus infection [66-70]. Remdesivir has been testified to treat the first US case of COVID-19 effectively [71]. Chloroquine has been used to treat malaria for so many years, have great potential to treat COVID-19 [72-75]. A combination of remdesivir and chloroquine was proven to effectively inhibit the recently emerged SARS-CoV-2 *in vitro* [19].

The present treatments mainly attentive on symptomatic and respiratory support for COVID-19 patient [76]. The extracorporeal membrane oxygenation (ECMO) commended by WHO to patients with refractory hypoxemia [77]. The convalescent plasma and IgG are delivered for some critical rescue treatment.

10. CONCLUSIONS

The COVID-19 has spread rapidly since it was first identified in WUHAN and it has spread to 203 countries as on June 2020. The characterization of novel coronavirus is in progress, researchers are extensively working on potential treatments and vaccination. In the present review, we have summarized the current informations about SARS-CoV-2 including origin, emergence, etiology, epidemiology, morphological and genetical assessment, viral transmission, pathogenicity, diagnostic criteria, clinical symptoms and current therapies for COVID-19 along with the recent updates. The review will help the researchers to know better about CoV-2 for further investigation.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. WHO - Coronavirus disease (COVID-2019) situation reports. Situation report—55. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200315-sitrep-55-covid-19.pdf?sfvrsn=33daa5cb_6.
2. Yu-Tao Xiang, Li W, Zhang Q, Jin Y, Rao W, Zhen L, Grace K I Lok, Ines HI chow, Cheung T and Hall BJ . Timely Research papers about COVI – 19 in China. 2020
3. Bogoch A, Watts A, Thomas-Bachli C, Huber MUG, Kraemer K, Khan. Pneumonia of unknown etiology in wuhan, China: potential for international spreadvia commercial air travel, J. Trav. Med. 2020, https://doi.org/10.1093/jtm/taaa008.
4. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology inwuhan China: the mystery and the miracle, J. Med. Virol. 92 (4) (2020) 401–402,https://doi.org/10.1002/jmv.25678.
5. World Health Organization. Novel Coronavirus—Japan (ex-China). Available online: https://www.who.int/csr/don/16-january-2020-novel-coronavirus-japan-ex-china/en/ (accessed on 19 January 2020).
6. Menachery VD, Yount BL, Debbink K, Agnihothram S, Gralinski LE, Plante JA, Graham RL, Scobey T, Ge XY, Donaldson EF, et al. A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence. Nat. Med. 2020, 21, 1508–1513.
7. Menachery VD, Yount BL, Sims AC, Debbink K, Agnihothram SS, Gralinski LE, Graham RL, Scobey T, Plante JA, Royal SR, et al. SARS-like WIV1-CoV poised for human emergence. Proc. Natl. Acad. Sci. USA, 2020, 113, 3048–3053.
8. Wuhan Municipal Health Commision. Wuhan Municipal Health and Health Commission's Briefing on the Current Pneumonia Epidemic Situation in Our City. Available online: http://wjw.wuhan.gov.cn/front/web/ showDetail/2019123108989 (accessed on 19 January 2020).
9. Wuhan Municipal Health Commision. Wuhan Municipal Commission of Health and Health on Pneumonia ofNew Coronavirus Infection. Available online: http://wjw.wuhan.gov.cn/front/web/showDetail/2020012009077 (accessed on 20 January 2020).
10. De Wilde AH, Snijder EJ, Kikkert M, van Hemert MJ. Host factors in coronavirus replication. Curr Top Microbiol Immunol. 2018;419:1-42. doi:10.1007/82_2017_25.
11. Paules CI, Marston HD, Fauci AS. Coronavirus Infections—More Than Just the Common Cold. JAMA. 2020;323(8):707–708. doi:10.1001/jama.2020.0757

12. De Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol. 2016;14(8):523-534. doi:10.1038/nrmicro.2016.81.
13. Chen Y, Liu Q, Guo D. Emerging coronaviruses: genome structure, replication, and pathogenesis. J Med Virol. 2020, 92:418-423. 10.1002/jmv.25681.
14. Chan JF, Kok KH, Zhu Z, Chu H, To KK, Yuan S, Yuen KY. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. Emerg Microbes Infect. 2020, 9:221-236. 10.1080/22221751.2020.1719902.
15. Meo SA, Alhowikan AM, Al-Khlaiwi T, Meo IM, Halepoto DM, Iqbal M, Usmani AM, Hajjar W, Ahmed N. Novel coronavirus 2019-nCoV. Prevalence, biological and clinical characteristics comparison with SARS-CoV and MERS-CoV. Eur Rev Med Pharmacol Sci. 2020 Feb;24(4):2012-2019. doi: 10.26355/eurrev_202002_20379.
16. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. Nature. 2020. https://doi.org/10.1038/s41586-020-2008-3 [Epub ahead of print].
17. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020. https://doi.org/10.1038/s41586-020-2012-7.
18. Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, et al. From SARS to MERS, thrusting coronaviruses into the spotlight. Viruses. 2019;11(1):E59. https://doi.org/10.3390/v11010059.
19. Yan-Rong Guo, Qing-Dong Cao, Zhong-Si Hong, Yuan-Yang Tan, Shou-Deng Chen, Hong-Jun Jin, Kai-Sen Tan, De-Yun Wang and Yan Yan. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the Status.Military Medical Research (2020) 7:11. https://doi.org/10.1186/s40779-020-00240-0.
20. Wu A, Peng Y, Huang B, Ding X, Wang X, Niu P, et al. Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China. Cell Host Microbe. 2020. https://doi.org/10.1016/j.chom.2020.02.001.
21. Angeletti S, Benvenuto D, Bianchi M, Giovanetti M, Pascarella S, Ciccozzi M. COVID-2019: the role of the nsp2 and nsp3 in its pathogenesis. J Med Virol. 2020. https://doi.org/10.1002/jmv.25719.
22. Zhang L, Shen FM, Chen F, Lin Z. Origin and evolution of the 2019 novel coronavirus. Clin Infect Dis. 2020. https://doi.org/10.1093/cid/ciaa112.
23. WHO- Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. https://www.who.int/publicationsdetail/.
24. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Napoli RP. Feature, Evaluation and Treatment. Corona virus (COVID – 19). 2020.Ncbi.nlm.nih.gov/books/NBKSS4776/.
25. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2001316.
26. Lee PI, Hsueh PR. Emerging threats from zoonotic coronaviruses-from SARS and MERS to 2019-nCoV. J Microbiol Immunol Infect. 2020. https://doi.org/ 10.1016/j.jmii.2020.02.001.
27. Jia HP, Look DC, Shi L, Hickey M, Pewe L, Netland J, et al. ACE2 receptor expression and severe acute respiratory syndrome coronavirus infection depend on differentiation of human airway epithelia. J Virol. 2005;79(23):14614–21.
28. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS. J Virol. 2020. https://doi.org/10.1128/JVI.00127-20.
29. 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), https://doi.org/10.1128/JVI.00127-20.
30. Jaimes JA, Millet JK, Stout AE, Andre NM, Whittaker GR. A tale of two viruses: the distinct spike glycoproteins of feline coronaviruses, 2020.Viruses 12.
31. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020. https://doi.org/10.1038/s41586-020-2012-7.

32. Ren LL, Wang YM, Wu ZQ, Xiang ZC, Guo L, Xu T, et al. Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study, Chinese Med J .2020. https://doi.org/10.1097/CM9.0000000000000722.
33. Xia S, Zhu Y, Liu M, Lan Q, Xu W, Wu Y, et al. Fusion mechanism of 2019- nCoV and fusion inhibitors targeting HR1 domain in spike protein. Cell Mol Immunol. 2020. https://doi.org/10.1038/s41423-020-0374-2.
34. Yu F, Du L, Ojcius DM, Pan C, Jiang S. Measures for diagnosing and treating infections by a novel coronavirus responsible for a pneumonia outbreak originating in Wuhan, China. Microbes Infect. 2020. https://doi.org/10.1016/j. micinf.2020.01.003.
35. Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. Nat Microbiol. 2020. https://doi.org/10.1038/s41564-020-0688-y.
36. Sawicki SG, Sawicki DL. Coronavirus transcription: a perspective. Curr Top Microbiol Immunol. 2005;287:31–55.
37. Hussain S, Pan J, Chen Y, Yang Y, Xu J, Peng Y, et al. Identification of novel subgenomic RNAs and noncanonical transcription initiation signals of severe acute respiratory syndrome coronavirus. J Virol. 2005;79(9):5288–95.
38. Perrier A, Bonnin A, Desmarets L, Danneels A, Goffard A, Rouille Y, et al. The C-terminal domain of the MERS coronavirus M protein contains a trans- Golgi network localization signal. J Biol Chem. 2019;294(39):14406–21.
39. Zhang W, Du RH, Li B, Zheng XS, Yang XL, Hu B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerg Microbes Infect. 2020;9(1):386–9.
40. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol. 2004;203(2):631–7.
41. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020. https://doi.org/10. 1056/NEJMoa2002032.
42. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020. https://doi.org/10.1001/jama.2020.1585 [Epub ahead of print].
43. Poutanen SM, Low DE, Henry B, Finkelstein S, Rose D, Green K, et al. Identification of severe acute respiratory syndrome in Canada. N Engl J Med. 2003;348(20):1995–2005.
44. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497–506.
45. Lauren Martz. CRISPR-based diagnostics are poised to make an early debut amid COVID-19 outbreak. 2020. https://www.biocentury.com/article/304556/covid-19-could-give-crispr-diagnostics-their-first-proof-of-principle
46. Florian Krammer. Discusses New Coronavirus Serological Assay.2020. https://www.contagionlive.com/news/florian-krammer-phd-discusses-new-coronavirus-serological-assay.
47. National Health Commission of the People's Republic of China. Diagnosis and Treatment of Pneumonia Caused by 2019-nCoV (version 6). 2020.
48. Poutanen SM, Low DE, Henry B, Finkelstein S, Rose D, Green K, et al. Identification of severe acute respiratory syndrome in Canada. N Engl J Med. 2003;348(20):1995–2005.
49. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497–506.
50. American Roentgen Ray Society. "New CT scoring criteria for timely diagnosis, treatment of coronavirus disease (COVID-19)." ScienceDaily. ScienceDaily, 1 April 2020. <www.sciencedaily.com/releases/2020/04/200401150833.htm>.
51. Guoquan Huang, Tao Gong, Guangbin Wang, Jianwen Wang, Xinfu Guo, Erpeng Cai, Shirong Li, Xiaohu Li, Yongqiang Yu, Liangjie Lin. Timely Diagnosis and Treatment Shortens the Time to Resolution of

Coronavirus Disease (COVID-19) Pneumonia and Lowers the Highest and Last CT Scores From Sequential Chest CT. American Journal of Roentgenology, 2020; 1 DOI: 10.2214/AJR.20.23078.
52. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y et al. Early transmission dynamics in wuhan, China, of novel coronavirus-infected pneumonia, N. Engl. J. Med. 2020. https://doi.org/10.1056/NEJMoa2001316.
53. Lei JJ, Li J, Li X, Qi X. CT imaging of the 2019 novel coronavirus (2019-nCoV) pneumonia, Radiology . 2020. 200236, https://doi.org/10.1148/radiol. 2020200236.
54. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, Lancet 395 (10223). 2020. 497–506, https://doi.org/10.1016/S0140-6736(20)30183-5.
55. Wang W, Tang J, Wei F. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China.2020. J. Med. Virol. 92 (4),441–447, https://doi.org/10.1002/jmv.25689.
56. Carlos WG, Dela Cruz CS, Cao B, Pasnick S, Jamil S. Novel wuhan (2019-nCoV) coronavirus, Am. J. Respir. Crit. Care Med. 2020. 201 (4),7–8, https://doi.org/10. 1164/rccm.2014P7.
57. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, Lancet.2020. 395 (10223),507–513, https://doi.org/ 10.1016/S0140-6736(20)30211-7.
58. Liu Z, Xiao X, Wei X, Li J, Yang J, Tan H, et al. Composition and divergence of coronavirus spike proteins and host ACE2 receptors predict potential intermediate hosts of SARS-CoV-2. J Med Virol. 2020. https://doi.org/10. 1002/jmv.25726.
59. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020. https://doi.org/10. 1056/NEJMoa2002032.
60. Chowell G, Abdirizak F, Lee S, Lee J, Jung E, Nishiura H, et al. Transmission characteristics of MERS and SARS in the healthcare setting: a comparative study. BMC Med. 2015;13:210.
61. Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. N Engl J Med. 2003; 348(20):1986–94.
62. Assiri A, Al-Tawfiq JA, Al-Rabeeah AA, Al-Rabiah FA, Al-Hajjar S, Al-Barrak A, 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. 2013;13(9):752–61.
63. Wang H, Xiao X, Lu J, Chen Z, Li K, Liu H, et al. Factors associated with clinical outcome in 25 patients with avian influenza a (H7N9) infection in Guangzhou, China. BMC Infect Dis. 2016;16(1):534.
64. Wang W, Tang J, Wei F. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. J Med Virol. 2020;92(4): 441–7.
65. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a singlecentered, retrospective, observational study. Lancet Respir Med. 2020. https://doi.org/10.1016/s2213-2600(20)30079-5.
66. Takeuchi O, Akira S. Innate immunity to virus infection. Immunol Rev. 2009; 227(1):75–86.
67. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and Chloroquine Effectively Inhibit the Recently Emerged Novel Coronavirus (2019- nCoV) in Vitro, Cell research. Cvetkovic RS, Goa KL. Lopinavir/ritonavir: a review of its use in the management of HIV infection. Drugs.2020. 2003;63(8):769–802.
68. Arabi YM, Asiri AY, Assiri AM, Aziz Jokhdar HA, Alothman A, Balkhy HH, et al. Treatment of Middle East respiratory syndrome with a combination of lopinavir/ritonavir and interferon-β1b (MIRACLE trial): statistical analysis plan for a recursive two-stage group sequential randomized controlled trial. Trials. 2020;21(1):8.
69. Chu CM, Cheng VC, Hung IF, Wong MM, Chan KH, Chan KS, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. Thorax. 2004;59(3):252–6.
70. Lim J, Jeon S, Shin HY, Kim MJ, Seong YM, Lee WJ, et al. Case of the index patient who caused tertiary transmission of COVID-19 infection in Korea: the application of lopinavir/ritonavir for the treatment of COVID-19 infected pneumonia monitored by quantitative RT-PCR. J Korean Med Sci. 2020;35(6):e79.
71. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. First case of 2019 novel coronavirus in the United States. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2001191 [Epub ahead of print].

72. Aguiar ACC, Murce E, Cortopassi WA, Pimentel AS, Almeida M, Barros DCS, et al. Chloroquine analogs as antimalarial candidates with potent in vitro and in vivo activity. Int J Parasitol Drugs Drug Resist. 2018;8(3):459–64.
73. Savarino A, Boelaert JR, Cassone A, Majori G, Cauda R. Effects of chloroquine on viral infections: an old drug against today's diseases? Lancet Infect Dis. 2003;3(11):722–7.
74. Vincent MJ, Bergeron E, Benjannet S, Erickson BR, Rollin PE, Ksiazek TG, et al. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. Virol J. 2005;2:69.
75. Golden EB, Cho HY, Hofman FM, Louie SG, Schonthal AH, Chen TC. Quinoline-based antimalarial drugs: a novel class of autophagy inhibitors. Neurosurg Focus. 2015;38(3):E12.
76. National Health Commission of the People's Republic of China. Diagnosis and Treatment of Pneumonia Caused by 2019-nCoV (version 6). 2020. http://www.gov.cn/zhengce/zhengceku/2020-02/19/content_5480948.htm. Accessed 18 Feb 2020.
77. WHO. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. https://www.who.int/publicationsdetail/ clinical-management-of-severe-acute-respiratory-infection-when-novelcoronavirus-(ncov)-infection-is-suspected. Accessed 28 Jan 2020.