Chapter 11

Prevention and Control Strategies for SARS-CoV-2 Infection

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Abstract The population of 168 countries all over the world is struggling with the outbreak of COVID-19. The outbreak is declared as pandemic and public health emergency of international concern declared by WHO. SARS-CoV-2 responsible for the present health emergency exhibited close resemblance with SARS-CoV. Both the viruses are zoonotic and belong to a large family of viruses *Coronaviridae*. The complete virus particle is made up of four major structural proteins, namely spikes (S), nucleocapsid (N), membrane (M), and envelope (E) encoded by virus genome. The S protein of virus shows similarity to S protein of SARS-CoV. COVID-19 spreads from person to person, and this makes it more vulnerable for causing infection. Several efforts are taken to find prevention strategies for COVID-19. Researchers across the globe are working to find effective vaccination for SARS-CoV-2. There is no vaccine or medication available till date for COVID-19. Preventive measures such as social distancing, awareness, maintenance of hygiene, isolation, and movement restrictions can help in control of COVID-19 spread. Proper sanitization and cleaned and sanitized public transport can be effective in inhibiting the spread of the virus. In the present situation of medical emergency, cooperation and support by following advices from the WHO and government only facilitate everyone to come over.

Keywords Coronavirus · COVID-19 · Vaccine · SARS-CoV-2

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Abbreviations

BW CoV	Beluga Whale CoV
CoV	Coronavirus
COVID	Coronavirus disease
HCoV	Human coronavirus
IBV	Infectious bronchitis virus
MERS	Middle East respiratory syndrome
PEDV	Porcine epidemic diarrhoea virus
SADS-CoV	Swine acute diarrhoea syndrome-CoV
SARS	Severe acute respiratory syndrome
TGEV	Transmissible gastroenteritis virus
WHO	World Health Organization

11.1 Introduction

The SARS-COV 2 or COVID-19 is emerged as global pandemic declared by the WHO with 184,976 reported cases across 159 countries until March 18, 2020 and accounts for 7529 deaths globally (WHO). The severity of COVID-19 can be easily understood by the exponentially increasing cases worldwide. The virus affects respiratory system like other influenza viruses and appears as a major threat throughout the world after 1918 Spanish flu (H1N1) outbreak. COVID-19 is one of the highly infectious diseases with the ability to affect a large population globally and can cause severe impact on socioeconomic stability of the world. The emergence of SARS-CoV traces back to year 2003 from China, and again another mutant emerged in 2012 known as MERS from Saudi Arabia. All the three highly infectious strains of CoV are found to be zoonotic and transmitted from animals to people.

The SARS-CoV-2 is also believed to be spread from fish market of Wuhan China in November 2019 and was first reported in the last week of December 2019 in 59 people at Wuhan, Hubei, China. The strain was completely novel and unknown to scientific fraternity at the time of its outbreak. The novel coronavirus or COVID-19 is highly infectious and spread so fast through people-to-people contact. The emergence and re-emergence of zoonotic viral strains pose immense threat to the human population and need to be addressed strategically with rapid response (Menachery et al. 2018). The SARS-CoV-2 is a novel coronavirus and is classified into virus family of *Coronaviridae*. Coronaviruses belong to large *Coronaviridae* family of viruses causing infection leads from common cold to severe illness and respiratory diseases. As per the studies conducted by various research groups worldwide, the COVID-19 genome is in close similarity with bat coronavirus, and it belongs to beta coronavirus group of *Coronaviridae* family. The brief classification of the SARS-CoV-2 is depicted in Fig. 11.1 (Tekes and Thiel 2016; Ashour et al. 2020), and some of the major human illnesses causing CoVs are given in Table 11.1.

Fig. 11.1 Classification of SARS-CoV-2

Table 11.1 Coronaviruses causing infection in humans

S. No.	Coronavirus	Strain	Disease
1	229 E	Alpha CoV	Common cold and flu
2	NL 63		
3	OC 43	Beta CoV	Flu, severe respiratory syndrome, pneumonia
4	HKU1		
5	MERS-CoV		
6	SARS-CoV		
7	SARS-CoV-2/ COVID-19	Delta CoV	Severe acute respiratory syndrome, fever, dry cough, kidney failure, high transmission between person to person
8	IBV		

The emergence of COVID-19 has drawn very much attention of researchers and health professionals because of its high infection potential and novel structure. Researchers found the stability of SARS-CoV-2 on various surfaces and compared the same with SARS-CoV-1. The experimental data under varied circumstances on different surfaces are found to be similar for both the strains (van Doremalen et al. 2020). The experimental observation shows that alterations in the epidemiologic characteristics of both the viruses may arise due to other reasons. The high viral concentration in the upper respiratory tract in the patient and the potential of

COVID-19-infected individual to carry and spread the virus while being in asymptomatic condition are some probable reasons for high infection rate, making its control challenging (Bai et al. 2020; Zou et al. 2020).

COVID-19 is a single-stranded (ss) RNA virus consisting of 26–36 kb positive sense RNA genome. The complete virus particle is made up of four major structural proteins, namely spikes (S), nucleocapsid (N), membrane (M), and envelope (E) encoded by virus genome (Forni et al. 2017). The size of SARS-CoV-2-encoded proteins shows similarity to bat SARS-CoV. The important difference is longer length and structure of S protein of SARS-CoV-2 in comparison to SARS-CoV and bat SARS-CoV observed by researchers. These S proteins are very crucial for receptor binding, membrane fusion, internalization of the SARS-CoV-2, tissue tropism, and host array. This S protein may be utilized as vital target for vaccine development (Menachery et al. 2016; Ji et al. 2020; Kumar et al. 2020).

Extensive efforts are already taken to control COVID-19 spread and for the development of effective vaccines around the world. Scientists are working round the clock individually and in collaboration to get some effective solution for the severe pandemic occurred by COVID-19. The COVID-19 outbreak can be reduced and controlled only by maintaining self-hygiene, social distancing, and strong immunity until any vaccine or effective medication is found. The present chapter provides an insight into the prevention and control strategies for COVID-19 including vaccine development and control measures.

11.2 SARS-CoV-2 Vaccine Development

COVID-19 contains the largest RNA genome and has spike proteins which play very important role in host–virus interaction and infection. After entering into host cells, the viral genome translates into two large precursors, poly-proteins known as PP1a and PP1ab. These precursors further processed by ORF1a-encoded viral proteinases, PL pro (papain-like proteinases) and 3CL pro (3C-like proteinases) into 16 mature non-structural proteins, namely nsp1 to nsp16. These nsps perform several important functions in viral RNA replication and transcription, RNA polymerase, RNA-processing enzymes such as poly (U)-specific endoribonuclease, protease, helicase, 3′–5′ exoribonuclease, ribose 2′-O methyltransferase, adenosine diphosphate-ribose-1′′-phosphatase, and cyclic nucleotide phosphodiesterase (Narayanan et al. 2015). Additionally, these nsps have a major role in viral RNA replication and transcription. Due to the absence of proofreading mechanism during RNA recombination process in pre-existed coronaviruses strains, it may account to be responsible for the evolution of SARS-CoV-2. The S gene-encoding spike glycoproteins have the maximum recombination frequency (Ji et al. 2020; Kumar et al. 2020). Out of the three major proteins forming viral envelope, S and M are glycol proteins and the E is non-glycosylated protein. M and E proteins are essential for virus assembly, morphogenesis, and budding. The M protein comprises short N terminal glycosylated ectodomain with a long C terminal domain and three membrane

domains. On the other hand, S glycoprotein is a type 1 fusion viral protein which includes two heptad repeat regions HR-N and HR-C and forms protein ectodomain-surrounded coiled structure. Additionally, the S protein cleaves into two subunits S1 and S2 and facilitates receptor binding (at domain 270–510) and membrane fusion, respectively (Tripet et al. 2004; Yuen et al. 2007; Fehr and Perlman 2015; Narayanan et al. 2015; Kumar et al. 2020; Wan et al. 2005). Considering the importance of S protein in attachment with host cell and variation in sequence of S protein from SARS-CoV-1, S protein may be considered potential candidate for vaccine development. Systematic assessment identified that 380 amino acid substitutions between SARS-CoV-1, SARS like bat CoV, and SARS-CoV-2 may be responsible for functional and pathogenic divergence of SARS-CoV-2 (Wu et al. 2020).

The COVID-19 virus is traced till death in non-survivors, and the longest virus shedding of 37 days has been observed in survivors (Zhou et al. 2020). It shows the severity of COVID-19 and its high infection rate especially in elderly and immunocompromised or weak immunity individuals. Several pharmaceutical R&D units and researchers are working to develop vaccine for SARS-CoV-2 pandemic. Researchers are putting all efforts to find a solution for combating this novel coronavirus. Researchers across the globe are trying to develop SARS-CoV-2 vaccine by using approaches like whole virus vaccine, antibody vaccine, DNA vaccine, recombinant protein subunit vaccine, and mRNA vaccine (Dresden 2020). Currently, there is no approved vaccine available for SARS-CoV-2. Recently, mRNA 1273 investigational vaccine has been developed by NIAID scientists in collaboration with the biotechnology company Moderna, Inc., based in Cambridge, MA. The clinical trial began at Kaiser Permanente Washington Health Research Institute (KPWHRI) in Seattle, and part of National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health, is funding the trial on mRNA platform approved for human trial after its promising response in animal models (NIH). A team of researchers from The Hong Kong University of Science and Technology, Hong Kong, reported high genetic similarity between SARS-CoV (outbreak in 2003) and SARS-CoV-2. This genetic similarity leads researchers to determine experimental data for SARS-CoV-1 B-cell and T-cell epitopes derived from S and N proteins which map identically to SARS-CoV-2. In comparison to the non-structural proteins, the T-cell response against the structural proteins has been reported to be the most immunogenic in peripheral blood mononuclear cells of recovering SARS-CoV patients. Additionally, T-cell responses against the S and N proteins have been reported to be the most dominant and long-lasting (Li et al. 2008; Channappanavar et al. 2014; Ahmed et al. 2020). As no mutation was observed in the SARS-CoV-2 proteins and long-lasting T-cell response against S protein, immune targeting of these epitopes may provide protection against COVID-19 or SARS-CoV-2 (Ahmed et al. 2020). Similar study was also reported by researchers from CFAR, King George's Medical University, Lucknow, India, in which researchers found glycosylated S protein site as potential target for vaccine development due to the genetic similarity with SARS-CoV and Bat CoV (Kumar et al. 2020). Table 11.2

Table 11.2 Vaccine under development to combat SARS-CoV-2

S. No.	Platform	Type of vaccine	Developer	Current stage (clinical/ regulatory)
1	DNA	DNA plasmid	Zydus Cadilla	Preclinical
2	DNA	INO4800-DNA plasmid	Inovio Pharmaceutical	Preclinical
3	RNA	mRNA 1273	Moderna Inc. and NIAID	Clinical trial phase 1
4	RNA	mRNA	Curevac	Preclinical
5	Live attenuated virus	Deoptimized live attenuated virus	Codagenix	Preclinical
6	RNA	mRNA BNT162	Pfizer and BioNTech	Preclinical
7	Recombinant protein subunit	S protein	University of Georgia	Preclinical
8	Recombinant protein subunit	S protein	Novavax	Preclinical
9	Recombinant protein subunit	S protein	University of Queensland	Preclinical
10	Recombinant protein subunit	S protein	Clover Biopharmaceuticals	Preclinical
11	Whole virus	Live attenuated virus	Johnson & Johnson	Preclinical
12	Whole virus	Live attenuated virus	Codagenix	Preclinical
13	Protein subunit	Full-length S trimers/ nanoparticle + matrix M	Novavax	Preclinical
14	Protein subunit	S protein (baculovirus production)	Sanofi Pasteur	Preclinical
15	Replicating viral vector	Measles vector	Zydus Cadila	Preclinical
16	Replicating viral vector	Horsepox vector	Tonix Pharma/Southern Research	Preclinical
17	Protein subunit	S protein clamp	GSK Pharma	Preclinical
18	Protein subunit	S1 protein	Baylor, New York Blood Center, Fudan University	Preclinical
19	Antibody	Antibody-based vaccine	Eli Lilly with AbCelerra	Screening

Source: WHO, Medical News Today, precisionvaccination.com, NIH, [Pfizer.com](https://www.pfizer.com)

comprise of some of the vaccines under development in various pharma and R&D laboratories with the stage of vaccine.

The above given set of data is few of ongoing search for potential vaccine. Vaccine development is one of the typical processes and requires lot of efforts and

time. There are several vaccines under development for SARS-CoV-1 and MERS-CoV, and researches are still going on at various stages of clinical trials. The available advanced technology for virus genome sequencing and global emergency of pandemic expedite the process to develop vaccine at earliest. The potential vaccine may take more than a year to come on the market after getting all approvals. As once the researchers develop a vaccine, it must get approved from various agencies like FDA after which the vaccine is sent to three phases of clinical trial. In phase 1, a small group of people are selected to evaluate the safety and immune response for vaccine. After successful trial in phase 1, the vaccine is tested for phase 2 clinical trial on approximately few hundred people to analyse the dosage. In phase 3, the effectiveness and safety evaluation of the vaccine will be evaluated on a large population. Once the vaccine passes all the three phases, it successfully gets approval from the FDA and is released for use to combat against the pathogen.

11.3 Types of Coronavirus Vaccines

Since the inception of deadly coronavirus such as SARS-CoV in 2003–2004, the human coronaviruses drew very much attention of the researchers worldwide to find a solution. The emergence and transfer of zoonotic pathogens in humans become a great threat for human population. After a decade of SARS outbreak, MERS is emerged as another severe threat and continued infecting after its discovery in 2012 (Stockman et al. 2006). In 2020 coronavirus emerged in a new form and is standing in front of the whole humanity as a severe threat in the form of pandemic accountable for many lives across the globe. The timely containment and slow rate of transmission of SARS-CoV-1 and MERS helped to control its larger impact (Menachery et al. 2018). In context of SARS and MERS outbreaks, many vaccines were developed and tested. The majority of coronavirus vaccines studied or under development so far broadly comprise the following types:

1. Whole virus vaccine/live attenuated vaccine
2. Antibody-based vaccine
3. Small subunit-based vaccine
4. Vector-based vaccine
5. Nucleic acid-based vaccine

Live attenuated vaccines contain weakened or dead virus to induce immune response in individual recipient. The live virus vaccine sometimes develops complications in the receiver, but it provides a long-term immune response for the specific virus. Antibody-based vaccines contain monoclonal antibodies which are strain specific and provide limited range of protection. As per the studies carried out on coronavirus, it mutated many times and in the last 15–18 years, some species emerged as deadly virus. The protein subunit-based vaccines are one of the safest vaccines, providing protection to a wide range of virus strains by targeting viral S and N proteins which facilitate attachment and interaction of virus to host cells.

Table 11.3 Coronavirus vaccines

S. No.	Platform	Type of vaccine	Target virus	Developer	Current stage	References
1	DNA	INO-4700 DNA plasmid vaccine expresses S protein	MERS-CoV	Inovio Pharmaceuticals	Clinical trial phase 2	Inovio.com
2	DNA	GLS-5300	MERS-CoV	GeneOne Life Science and Inovio	Clinical trial phase 1	Shen et al. (2019)
3	Vector (adeno virus)	ChAdOx1 S protein antigen	MERS CoV	University of Oxford	Clinical trial phase 1	Alharbi et al. (2017)
4	Vector	Ad5-SARS-CoV vectors	SARS-CoV	University of Pittsburgh	Animal trial	Gao et al. (2003)
5	Live attenuated	UV-inactivated purified SARS-CoV	SARS-CoV	National Institute of Infectious Diseases Japan	Subclinical	Takasuka et al. (2004)

Nucleic acid-based vaccines also known as DNA or RNA vaccine are also safe for the recipients and provide long-term immunity. The mRNA-based vaccine for COVID-19 already sent for phase 1 clinical trial. Some of the coronavirus vaccines are listed in Table 11.3.

The research reported by various individual groups shows that CoV S subunit protein provides complete protection than SARS-CoV live attenuated vaccines, full-length S protein, and DNA-based S protein vaccines (Buchholz et al. 2004). The S protein gene of coronavirus is a highly preferable target of antigenicity as exhibited by the reactivity with convalescent SARS patient sera. It shows precise binding to soluble ACE-2 receptor. Additionally, it promotes antibody-dependent viral access in Raji B cells of human refractory B Cells and provokes defense against a impute infection in an animal model (Liu et al. 2020).

11.4 Efficacy and Effectiveness of Coronavirus Vaccines

The efficacy and effectiveness of vaccine are the most important criteria for the development of vaccine. The efficacy of a vaccine is defined as “The reduction percentage of disease in vaccinated or recipients’ group in comparison to unvaccinated groups under optimal condition.” Whereas, the effectiveness of a vaccine is defined as “The percentage control achieved for particular disease in vaccinated group compared to unvaccinated group at real world in natural environment.” The efficacy of vaccine is studied when the vaccine is in clinical trial, whereas the effectiveness is studied after the release of vaccine commercially or to mass after all approvals.

The efficacy of different types of coronavirus vaccines is studied for their potential application in the prevention of the disease. Various types of coronavirus vaccines are under research like inactivated coronavirus, live attenuated coronavirus, S-protein-based, vectored vaccines, DNA vaccines, and combination vaccines. Vaccines for combating several animal-based CoVs have been developed and demonstrated to be efficient in averting viral contagion. Vaccines for human CoVs, especially deadly SARS-CoV-1, MERS-CoV, and the present pandemic COVID-19, are under development in various levels of preclinical, subclinical, and clinical trials. The study of virus-like particle vaccine in mice and whole virus vaccine in non-human primates and ferrets exhibits immune response against CoV infection, but later on vaccinated animals unveiled immunopathological lung disease (Tseng et al. 2012). Another study in canine CoV vaccine exhibited that the vaccination with inactivated CoV can expressively reduce the viral replication followed with the reduction in occurrence of clinical symptoms and disease due to virulent CoV infection (Fulker et al. 1995). In a study carried out on rhesus monkey with SARS-CoV, inactivated vaccine exhibited effective concomitant humoral and mucosal immunity against SARS-CoV infection. The rhesus monkey was inoculated with a varied dose (0.5, 5, 50, and 5000 µg) of vaccine and provided with booster dose after a week. Afterwards the animals were exposed to NS-1 strain of SARS-CoV, the vaccinated monkeys had not shown any systematic side effects neither any clinical symptoms. The vaccine in study shows promising results on monkeys and may be further tested under clinical trials on humans (Zhou et al. 2005).

Various therapeutic efforts were adopted for the CoV vaccine globally; however, no solution in form of promising treatment or vaccination is identified till date. Progressive efforts on developed animal models and under clinical trials are ongoing to find an effective vaccine that is underway. As discussed in the above sections, targeting S glycoproteins of the virus and its subunits responsible for host interaction may be effective target for CoV vaccine for humans. As per research conducted on various CoV genetic structure, the S protein genetic make-up is found to be similar in SARS-CoV, bat SARS-CoV, and SARS-CoV-2. Previously conducted studies on SARS-CoV and MERS-CoV vaccine development based on S glycoproteins of virus can provide insight into effective and efficient vaccine development against deadly strains of corona.

11.5 Control Strategies of Coronavirus Infection

The viral diseases are emerging as serious threat to public health in the past 20 years. Several viral epidemics identified as potential health hazard such as SARS-CoV, H1N1, H5N1 influenza, MERS-CoV, Zika, Ebola, and now COVID-19 erupt as pandemic affecting approximately 168 countries around the globe. The outbreak of SARS-CoV-2 is identified as public health emergency of international concern declared by WHO. The reported potential of human-to-human transmission of the virus makes it a more vulnerable threat for a large population. COVID-19 is a serious

global health issue, and scientists across the world are working tirelessly to find its prevention and therapeutic strategies. As of now, no medication or vaccine is available for COVID-19. The symptomatic treatment in mild infections and oxygen therapy in critical cases are found to be effective. There are some reports providing positive response from the use of individual and combination of drugs like ritonavir, chloroquine, lopinavir, BCX-4430 (salt form of galidesivir), nitazoxanide, and ribavirin (Liu et al. 2020). But no fundamental or approved evidence is available for the use of these drugs till date from any international organization like the WHO or FDA.

Presently, only precautionary measures and efficient health response from governments, doctors, and public can only prevent COVID-19 infection from spreading. Person-to-person transmission of virus is critical, and super spreading events can occur in public gathering. Some of the important steps which need to be taken to prevent spreading of COVID-19 in population are as follows:

- (a) Isolation of the affected person and individual travelling from affected countries or potential carriers. As some of the studies suggested that COVID-19 can be spread via asymptomatic carriers too, and it is a dangerous situation.
- (b) Imposing travel restrictions from and to the affected countries.
- (c) Blocking transmission by maintaining high-level hygienic condition in home and surroundings.
- (d) Avoid social gathering, as it inhibits its geometrical progression and flatten the curve.
- (e) Spreading awareness among public.
- (f) Use of masks and protective clothes by infected, elderly, and immunocompromised individuals to avoid spread of infection or from protecting self from COVID-19.
- (g) Maintenance of good immunity, consumption of nutrient diet, consumption of vitamins especially C and E with yoga and exercises help in fighting with COVID-19 infection.
- (h) Social distancing, as the virus can transmit from person to person, i.e., maintenance of social distance, is highly recommended.

SARS-CoV-2 is a novel virus, and very less is known about the virus. Precaution is better than cure perfectly fits for COVID-19.

“Natural calamities bring people closer, viral calamities keep people away.”

Executive Summary

- As per WHO, 209,839 people are affected by COVID-19 until March 20, 2020.
 - COVID-19 is accountable for 8778 death and is present in 168 countries worldwide.

(continued)

- Several studies are going on for exploring efficient medication and vaccine for COVID-19.
 - S-glycoprotein-based and mRNA-based vaccines show prominent response.
- SARS-CoV-2 shows similarity to SARS-CoV and bat-CoV.
 - The similarity in genome structure especially in S protein can be utilized for vaccine development and alternate medications which are effective on SARS-CoV.
- Precaution is only cure is true in the case of COVID-19.
 - Maintenance of social distancing, hygiene, and isolation.
 - Social awareness by government, media, NGOs, and responsible citizens.
 - Isolation of infected, suspected, and possible asymptomatic carriers.
 - Total lock down in highly affected places.
 - Proper maintenance of clean and sanitized environment.
- COVID-19 is a novel virus, and proper precautions is the only cure.
 - Support to government and responsible agencies by following advisory and guidelines.
 - Follow all the instructions and guidelines released by the WHO.

11.6 Conclusions

COVID-19 or SARS-CoV-2 is a novel virus having close genetic resemblance with SARS-CoV and bat-CoV. The virus is highly infectious and can transfer from person to person. As predicted previously by various researchers worldwide, COVID-19 emerged as pandemic. The present situation clearly calls for the fast and efficient availability of COVID-19 vaccines and therapeutics. Worldwide scientists already are working tirelessly for efficient and effective solution of COVID-19 pandemic; meanwhile, it is moral and social obligation of each individual on the planet to follow the guidelines and advisory from the government, the WHO, and other responsible agencies. Extended support and cooperation from public can only help to control the spread of COVID-19 further.

11.7 Future Perspective

1. An in-depth study to understand SARS-CoV-2 needs to be done.
2. Development of efficient vaccines and therapeutics/antiviral drugs needs to be carried out at the earliest.
3. Fast, cost-effective, and accurate diagnostic kits need to be developed.
4. The virus exhibits strong opportunity to study viral mutation pattern and their fast emergence as novel viral particle.
5. Nanomaterial-based drug delivery and diagnostics need to be explored for efficient and effective delivery and diagnostics.

References

- Ahmed SF, Quadeer AA, McKay MR (2020) Preliminary identification of potential vaccine targets for the COVID-19 coronavirus (SARS-CoV-2) based on SARS-CoV immunological studies. *Viruses* 12(3):254
- Alharbi NK, Padron-Regalado E, Thompson CP, Kupke A, Wells D, Sloan MA, Grehan K, Temperton N, Lambe T, Warimwe G, Becker S, Hill AVS, Gilbert SC (2017) ChAdOx1 and MVA based vaccine candidates against MERS-CoV elicit neutralising antibodies and cellular immune responses in mice. *Vaccine* 35(30):3780–3788
- Ashour MH, Elkhatib FW, Rahman MM, Elshabrawy AH (2020) Insights into the recent 2019 novel coronavirus (SARS-CoV-2) in light of past human coronavirus outbreaks. *Pathogens* 9(3). <https://doi.org/10.3390/pathogens9030186>
- Bai Y, Yao L, Wei T, Tian F, Jin D-Y, Chen L, Wang M (2020) Presumed asymptomatic carrier transmission of COVID-19. *JAMA*. <https://doi.org/10.1001/jama.2020.2565>
- Buchholz UJ, Bukreyev A, Yang L, Lamirande EW, Murphy BR, Subbarao K, Collins PL (2004) Contributions of the structural proteins of severe acute respiratory syndrome coronavirus to protective immunity. *Proc Natl Acad Sci U S A* 101(26):9804–9809
- Channappanavar R, Fett C, Zhao J, Meyerholz DK, Perlman S (2014) Virus-specific memory CD8 T cells provide substantial protection from lethal severe acute respiratory syndrome coronavirus infection. *J Virol* 88(19):11034
- van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, Tamin A, Harcourt JL, Thornburg NJ, Gerber SI, Lloyd-Smith JO, de Wit E, Munster VJ (2020) Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N Engl J Med*. <https://doi.org/10.1056/NEJMc2004973>
- Dresden D (2020) Coronavirus vaccine: everything you need to know. 12 March 2020. Available from <https://www.medicalnewstoday.com/articles/coronavirus-vaccine>
- Fehr AR, Perlman S (2015) Coronaviruses: an overview of their replication and pathogenesis. In: Maier HJ, Bickerton E, Britton P (eds) *Coronaviruses: methods and protocols*. Springer New York, New York, pp 1–23
- Forni D, Cagliani R, Clerici M, Sironi M (2017) Molecular evolution of human coronavirus genomes. *Trends Microbiol* 25(1):35–48
- Fulker R, Wasmoen T, Atchison R, Chu HJ, Acree W (1995) Efficacy of an inactivated vaccine against clinical disease caused by canine coronavirus. In: Talbot PJ, Levy GA (eds) *Corona- and related viruses: current concepts in molecular biology and pathogenesis*. Springer US, Boston, MA, pp 229–234
- Gao W, Tamin A, Soloff A, D’Aiuto L, Nwanegbo E, Robbins PD, Bellini WJ, Barratt-Boyes S, Gambotto A (2003) Effects of a SARS-associated coronavirus vaccine in monkeys. *Lancet* 362(9399):1895–1896

- Ji W, Wang W, Zhao X, Zai J, Li X (2020) Cross-species transmission of the newly identified coronavirus 2019-nCoV. *J Med Virol* 92(4):433–440
- Kumar S, Maurya VK, Prasad AK, Bhatt MLB, Saxena SK (2020) Structural, glycosylation and antigenic variation between 2019 novel coronavirus (2019-nCoV) and SARS coronavirus (SARS-CoV). *Virus Dis* 2020:1–9. <https://doi.org/10.1007/s13337-020-00571-5>
- Li C K-f, Wu H, Yean H, Ma S, Wang L, Zhang M, Tang X, Temperton NJ, Weiss RA, Brenchley JM, Douek DC, Mongkolsapaya J, Tran B-H, Lin C-l S, Screaton GR, Hou J-l, McMichael AJ, Xu X-N (2008) T cell responses to whole SARS coronavirus in humans. *J Immunol* 181(8):5490
- Liu C, Zhou Q, Li Y, Garner LV, Watkins SP, Carter LJ, Smoot J, Gregg AC, Daniels AD, Jervsey S, Albaui D (2020) Research and development on therapeutic agents and vaccines for COVID-19 and related human coronavirus diseases. *ACS Cent Sci* 6(3):315–331
- Menachery VD, Yount BL, Sims AC, Debbink K, Agnihothram SS, Gralinski LE, Graham RL, Scobey T, Plante JA, Royal SR, Swanstrom J, Sheahan TP, Pickles RJ, Corti D, Randell SH, Lanzavecchia A, Marasco WA, Baric RS (2016) SARS-like WIV1-CoV poised for human emergence. *Proc Natl Acad Sci U S A* 113(11):3048
- Menachery VD, Gralinski LE, Mitchell HD, Dinnon KH, Leist SR, Yount BL, McAnarney ET, Graham RL, Waters KM, Baric RS (2018) Combination attenuation offers strategy for live attenuated coronavirus vaccines. *J Virol* 92(17):e00710–e00718
- Narayanan K, Ramirez SI, Lokugamage KG, Makino S (2015) Coronavirus nonstructural protein 1: common and distinct functions in the regulation of host and viral gene expression. *Virus Res* 202:89–100
- Shen X, Sabir JSM, Irwin DM, Shen Y (2019) Vaccine against Middle East respiratory syndrome coronavirus. *Lancet Infect Dis* 19(10):1053–1054
- Stockman LJ, Bellamy R, Garner P (2006) SARS: systematic review of treatment effects. *PLoS Med* 3(9):e343
- Takasuka N, Fujii H, Takahashi Y, Kasai M, Morikawa S, Itamura S, Ishii K, Sakaguchi M, Ohnishi K, Ohshima M, Hashimoto S-i, Odagiri T, Tashiro M, Yoshikura H, Takemori T, Tsunetsugu-Yokota Y (2004) A subcutaneously injected UV-inactivated SARS coronavirus vaccine elicits systemic humoral immunity in mice. *Int Immunol* 16(10):1423–1430
- Tekes G, Thiel HJ (2016) Chapter 6—Feline coronaviruses: pathogenesis of feline infectious peritonitis. In: Ziebuhr J (ed) *Advances in virus research*, vol 96. Academic Press, Cambridge, MA, pp 193–218
- Tripet B, Howard MW, Jobling M, Holmes RK, Holmes KV, Hodges RS (2004) Structural characterization of the SARS-coronavirus spike S fusion protein core. *J Biol Chem* 279(20):20836–20849
- Tseng C-T, Sbrana E, Iwata-Yoshikawa N, Newman PC, Garron T, Atmar RL, Peters CJ, Couch RB (2012) Immunization with SARS coronavirus vaccines leads to pulmonary immunopathology on challenge with the SARS virus. *PLoS One* 7(4):e35421
- Wan XF, Ataman D, Xu D (2005) Application of computational biology in understanding emerging infectious diseases: Inferring the biological function for S-M complex of SARS-CoV. *Prog Bioinformatics*. Nova Science Publishers, New York, pp 55–80
- Wu A, Peng Y, Huang B, Ding X, Wang X, Niu P, Meng J, Zhu Z, Zhang Z, Wang J, Sheng J, Quan L, Xia Z, Tan W, Cheng G, Jiang T (2020) Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China. *Cell Host Microbe* 27(3):325–328
- Yuen K-Y, Wong SSY, Peiris JSM (2007) The severe acute respiratory syndrome. In: Fong IW, Alibeck K (eds) *New and evolving infections of the 21st century*. Springer New York, New York, pp 163–193
- Zhou J, Wang W, Zhong Q, Hou W, Yang Z, Xiao S-Y, Zhu R, Tang Z, Wang Y, Xian Q, Tang H, Wen L (2005) Immunogenicity, safety, and protective efficacy of an inactivated SARS-associated coronavirus vaccine in rhesus monkeys. *Vaccine* 23(24):3202–3209

- Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 395 (10229):1054–1062
- Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, Yu J, Kang M, Song Y, Xia J, Guo Q, Song T, He J, Yen H-L, Peiris M, Wu J (2020) SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med* 382(12):1177–1179