MATERIALS FOR DIAGNOSIS, PREVENTION AND CONTROL OF COVID-19 PANDEMIC

Vamsi Krishna Kudapa[1], Nirlipta Priyadarshini Nayak[2], Rajeev Gupta[3*]

[1]Department of Chemical Engineering, [2]Department of Petroleum Engineering and Earth Science, [3]Department of Physics, College of Engineering Studies, University of Petroleum & Energy Studies, Dehradun-248007, Uttarakhand, India.

*** Address correspondence to:**

Dr. Rajeev Gupta, College of Engineering Studies, University of Petroleum & Energy Studies, Dehradun-248007, Uttarakhand, India.

Tel/Fax: +91 8126130342

Mobile: +91 9897716629

Email: rajeev@ddn.upes.ac.in

Abstract

The coronavirus infection disease 2019 (COVID-19) pandemic is causing an extreme effect on the worldwide society and economy. The episode of COVID-19 poses various challenges that include diagnosis, prevention and proper medication. Hence, most national governments across the globe have advised to accelerate the advancement of biomaterials and techniques for the development of effective diagnosis, therapeutics and control of COVID-19. This study endeavors to give a point of view on how the improvement of novel materials can assist researchers with handling the difficulties with COVID-19 and mitigate the challenges.

E-Mail: rajeev@ddn.upes.ac.in

Introduction

The serious respiratory disorder as a result of the 2019 novel coronavirus (2019-nCoV) which is also called coronavirus 2 (SARS-CoV-2) has been increasing exponentially worldwide since the origination of the disease in Wuhan City of Hubei Region of China [1]. Coronaviruses are a cluster of viruses belonging to the clan Coronaviridae, which has an average radius of 60 nm. Some virus uses animals as the initial host for spreading and then gradually move their way to infect humans also. Predecessors to MERS and SARS coronaviruses were seen in mammals, especially in bats. Researchers showed that SARS virus made up their way from bats to nocturnal, small mammals (also called civets) and to human beings. Research evidence has shown that coronavirus originated from bats, which then transmitted through an in-between carrier. Although scientists have not yet recognized the transmittable intermediary creature [2]. Figure 1 represents four structural proteins that includes spike envelop membrane nucleocapsid.
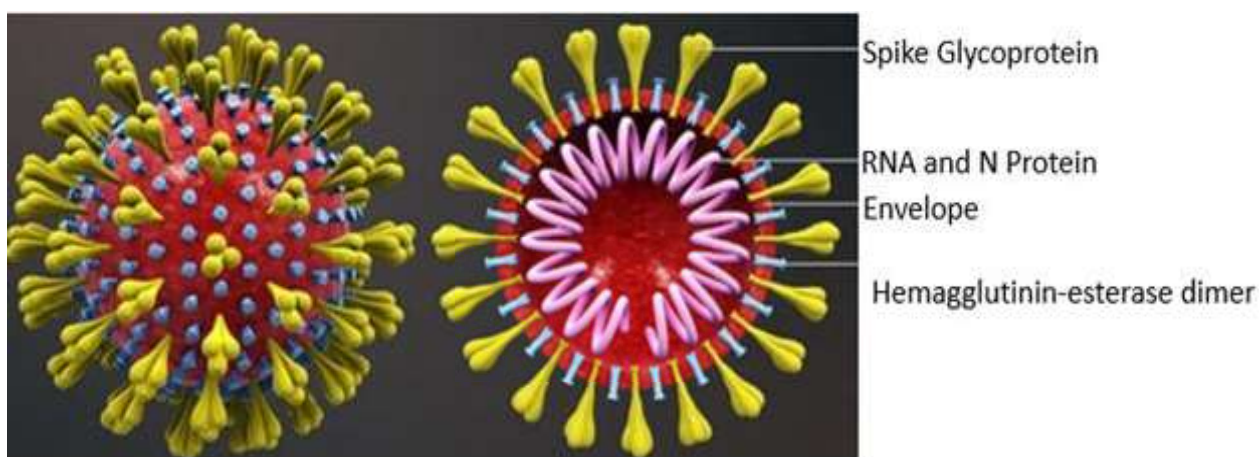
*Figure 1: Schematic of four structural protein's in covid-19 (**Source:** https://commons.wikimedia.org/wiki/File:3D_medical_animation_corona_virus.jpg).*

The first case of corona virus was reported in the winter of 1960. In 2001, a Canadian research team reported nearly 500 patients with Flu-like symptoms that showed that corona virus strain was infested in 17-18 cases by a polymerase chain reaction. At the first stage, the corona was observed as a normal non-lethal virus [3]. Subsequently, in 2003, numerous studies reported evidences showing the spread of coronavirus in countries mostly in the United States America, Vietnam, Taiwan, Hong Kong and Thailand. Figure 2 shows various pandemics that occurred before COID 19, such as Spanish flu in 1918, Hong Kong flu in 1968 and Pandemic flu in 2009 along with their mortality rates. Numerous cases of a serious respiratory disorder triggered by coronavirus were reported in 2003 and a high mortality rate was reported with more than 1000 patients. A continuous daily testing of 1000's continuous testing revealed the complications.
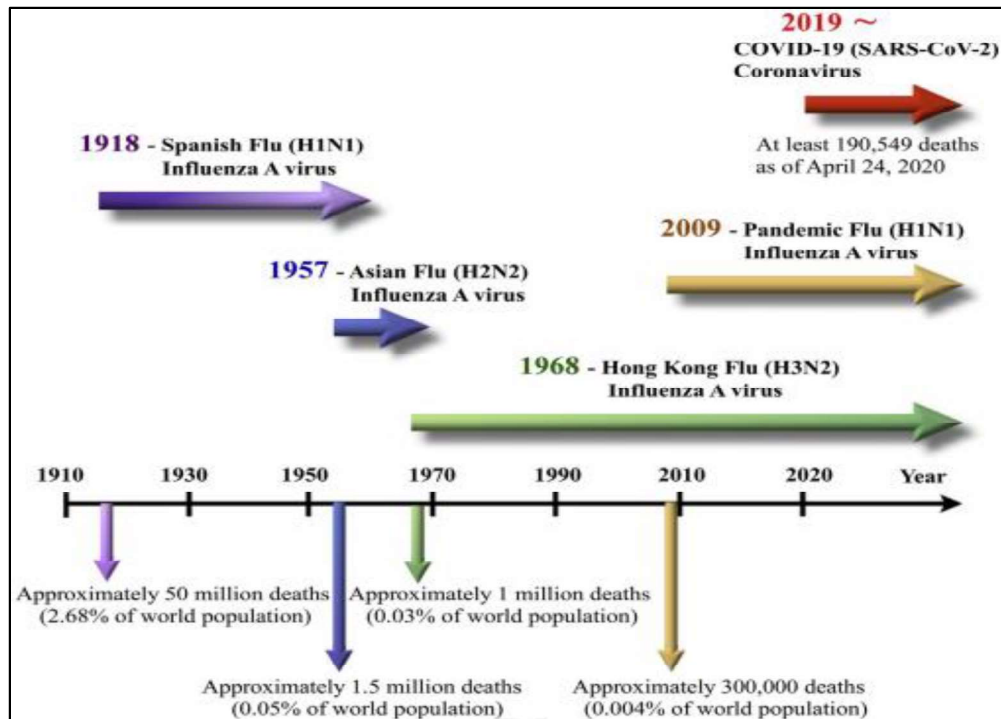
Figure 2: History of different pandemics during different periods since 1918 and virus spread afterward (**Source:** Biomedical (2020)).
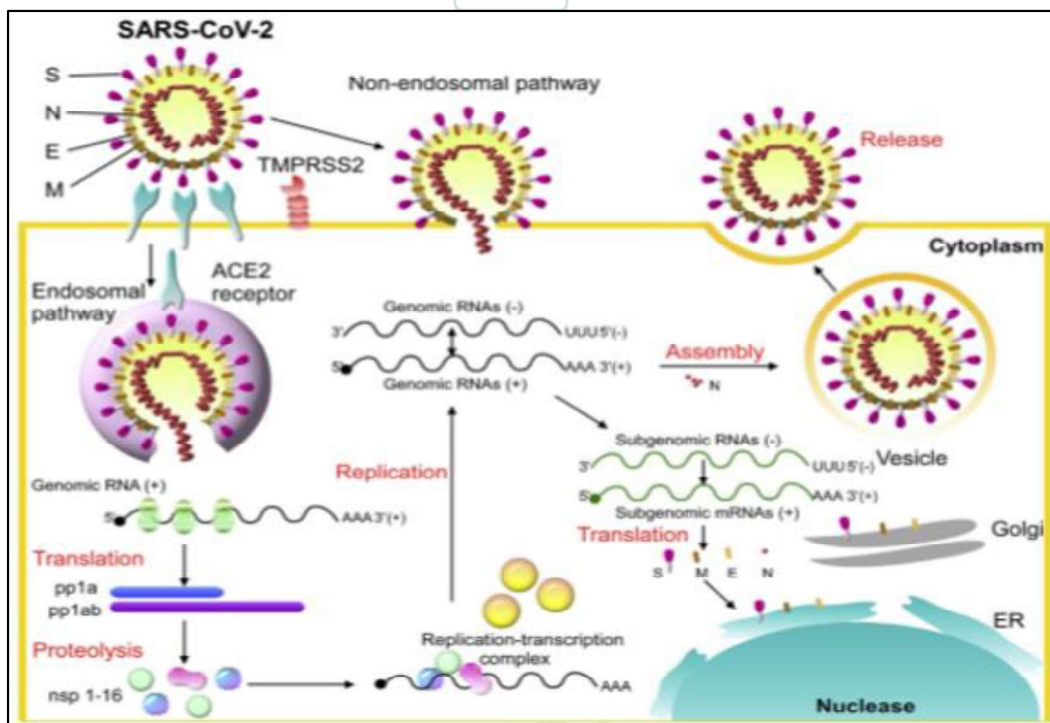

Figure 3: Schematic representing the lifecycle of SARS-CoV-2 (**Source:** Biomedical (2020)).

Further research concluded and recognized the pathogenesis of the disease and exposed it as coronavirus. Consequently, in 2004, WHO and centers for disease control and prevention acknowledged as "state of emergency" with 50 patients of serious respiratory disorders was reported during a study conducted in Hong Kong. It was found from the study that 30 out of 50 were infected with the deadly corona virus. In 2012, several infected patients and deaths were presented in reports published in Saudi Arabia. The COVID-19 first case was reported and quarantined from a pneumonia infected patient who was a resident in Wuhan, china [4].

Figure 3 represents the putative life pattern of SARS CoV- 2 in swarm cells that starts from spike protein and hACE2 receptor binding. The conformational change in the S protein after receptor binding encourages viral envelope combination with the cell layer through the endosomal pathway. The viral RNA genome is then discharged into the cytoplasm and deciphered into viral replicas polyproteins pp1a and 1ab, which can be divided into little items by infection-encoded proteinases. The polymerase translates a progression of sub genomic mRNAs by intermittent record. The sub genomic mRNAs are finally converted into viral auxiliary proteins. The S, E and M proteins enter the endoplasmic reticulum (ER), Golgi device, and the N protein is joined with the positive-abandoned genomic RNA to shape a nucleoprotein complex. The auxiliary proteins and nucleoprotein complex are collected with the viral envelope at the ER-Golgi middle of the road compartment. The recently collected viral particles are then discharged from the contaminated cell.

COVID-19 -Source and Transmission

In December 2019, unidentified cases of severe pneumonia were reported in adults to local hospitals from Wuhan, the major transportation hub of China and the capital city of Hubei region. The observation system, which was activated after the SARS outburst in addition to respiratory samples that were obtained from the carriers or infected and were subsequently directed to laboratories for etiologic inquiries. The outburst was reported to the World Health Organization by China on December 31st, 2019. The virus was later recognized as coronavirus on 7th January, which had homology with the bat coronavirus and similarity with the SARS CoV. Samples which were collected from the wuhan seafood marketplace also confirmed positive, indicating that coronavirus was initiated from china [5]. The number of cases exponentially surged up even without cases that were not found to have any exposure with the live animal market. This supported the theory that human-human interaction was the main reason for this spreading[6]. It was suspected that the Chinese New Year celebration fueled the widespread cases due to the massive gathering of people. Countries such as Japan, South Korea and Thailand (outlying areas of China) had subsequently numerous cases that were found in people who were coming back to their country from Wuhan. On 20th Jan 2020 transmission to healthcare workers who were the caretakers for the patients was pronounced. Population of Wuhan (11

million) were put under containment zone and were under complete lockdown with restrictions in and out of Wuhan. The lockdown was forced in other cities of Hubei region due to the critical risk of spreading the disease. Some countries outside China also reported cases of COVID-19 which confirmed that a native human-human outburst was happening in those countries [7]. Other countries including India initiated screening processes at airports to find symptomatic people with symptoms (symptomatic) who were coming back from China mainly. Further, countries including India took drastic measures such as evacuation of citizens from Wuhan and they were placed in isolation for 14 days followed by rapid testing that was done for the virus.

Figure 4 represents the key sources through which corona virus will spread from animals to humans and then from human-human transfer.
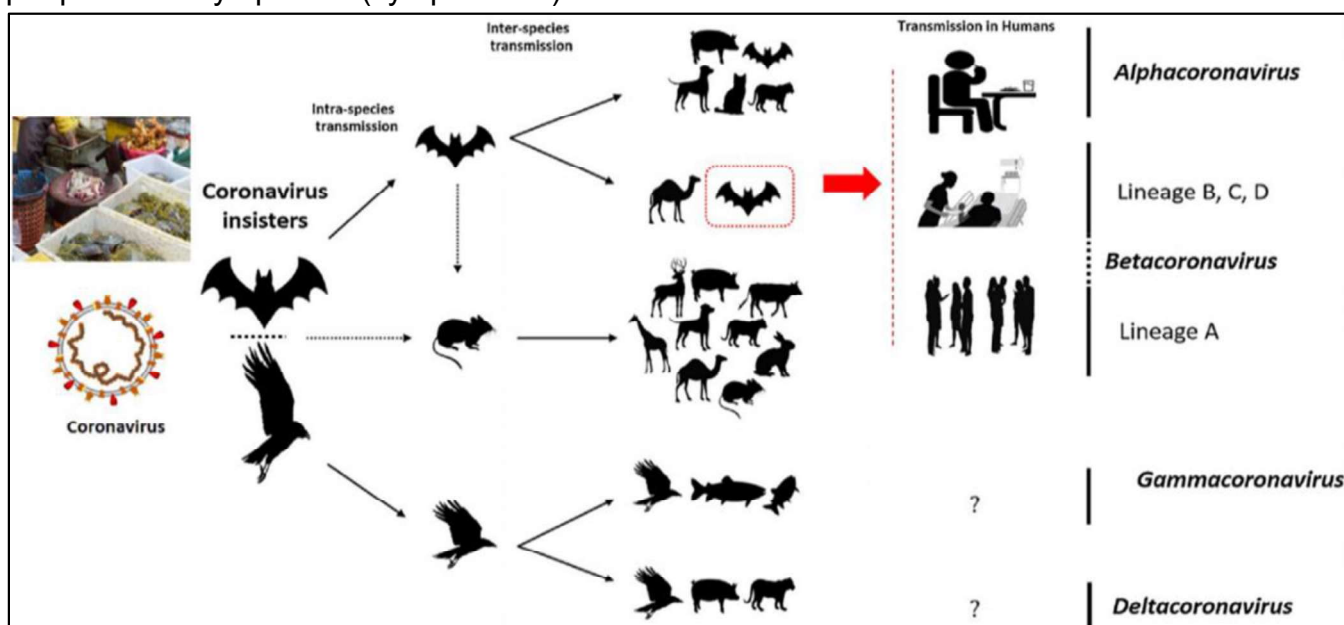

*Figure 4: Transmission cycle of -COVID 19 from origin to allover the globe (**Source:** Journal of Advanced Research (2020)).*

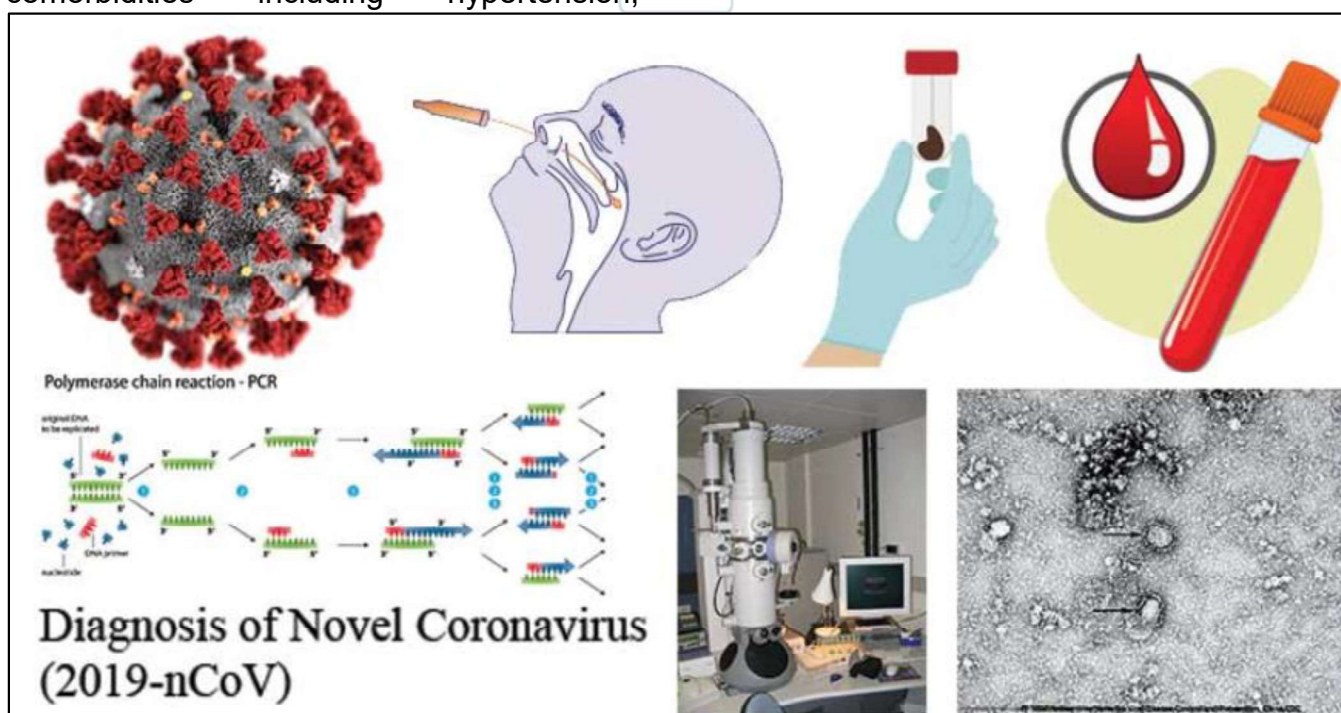**Identification/Diagnosis of COVID-19**

Prior to the cases of SARS-CoV, human CoVs were believed to lead a self-limiting lower respiratory infection and cold-like upper respiratory infection [9]. Corona virus-infected first death in china was reported by a patient who was in isolation for SARS-CoV with acute pneumonia [10]. It was found that, there were some resemblances in the medical features of infection induced by COVID-19 as in previous beta-CoVs and other respiratory infection viruses [11]. Similar to MERS-CoV and SARS-CoV, which triggered epidemics in the earlier years [9], shortness of breath, cough and common fever were reported as the initial symptoms of COVID-19[6]. Diarrhea was also reported in

about 20–25% of patients with MERS-CoV and SARS-CoV infection [9]. However, intestinal symptoms have rarely been reported in patients with COVID-19[6]. In addition to previous findings another medical study conducted with a total of 99 patients have testified chest pain, nausea vomiting and confusion were found. Bilateral or Unilateral association companionable with viral pneumonia was established on thorax CT imaging or x-rays of the examined patients, bilateral multiple lobular and sub-segmental consolidation areas were detected in patients admitted in the ICU. Fatigue, Dry-cough, fever and myalgia indications were stated most in a research report that studied 41 patients that were hospitalized; with fewer, indications of expectoration, hemoptysis, hemoptysis, diarrhea, and headache were correspondingly detected. Further, nearly half of these patients were found with comorbidities including hypertension, cardiovascular disease and underlying diabetes mellitus.

The patients with underlying comorbidity exhibited a more critical situation that was derived from the knowledge expanded after the past epidemics. For instance, in MERS and SARS, the identification of n-CoV 2019 infection was established on rapid spread through human interaction, travelling and detailed laboratory testing. The analytic tools that are used include viral cultures, serology and molecular methods. The diagnostic methods, which were used commonly, are molecular methods such as real-time PCR or reverse transcription-polymerase chain reaction (RT-PCR). The samples were prepared with RNA that was acquired from respiratory samples such as sputum, nasopharyngeal aspirates, oropharyngeal swabs, broncho-alveolar lavage or deep tracheal aspirates [Figure 5].

Figure 5: Diagnosis of covid-19 with the Polymerase Chain Reaction (PCR) (**Source:** https://www.civilsdaily.com/news/pcr-test-for-diagnosis-of-the-covid-19/).

To be specific, lower respiratory tract samples offers a considerably greater genome fraction and viral load than upper respiratory tract samples. The mentioned procedures are constructive under the condition of calculating results rapidly, presenting the structure of genome and viral load. The dependency of antibody finding is normally lesser because of sensitivity compared to the molecular methods and it is regularly applied in reflective diagnosis. Viral culture is considered as a time-consuming technique if matched with other techniques. So this is considered more beneficial at the initial phase of epidemic before other indicative techniques became medically available [12]. For vaccine evaluation trials and in-vivo and in-vitro antiviral treatment, vaccine cultures can be used.

Bhardwaj et al [13] simulated the effect of surface wettability, relative humidity and ambient temperature on the aeration time of the droplet at two altered temperatures, 25o C and 40oC outdoors in summer and inside a room with air-conditioning at humidity as 50o and 30%, respectively. The evaporation time is directly proportional to the droplet's radius or two-third the power of volume and inversely proportional to the temperature, for a 15oC rise in temperature about 50% and probably the probability of contamination through interaction with an infected droplet reduced with the rise in ambient temperature.
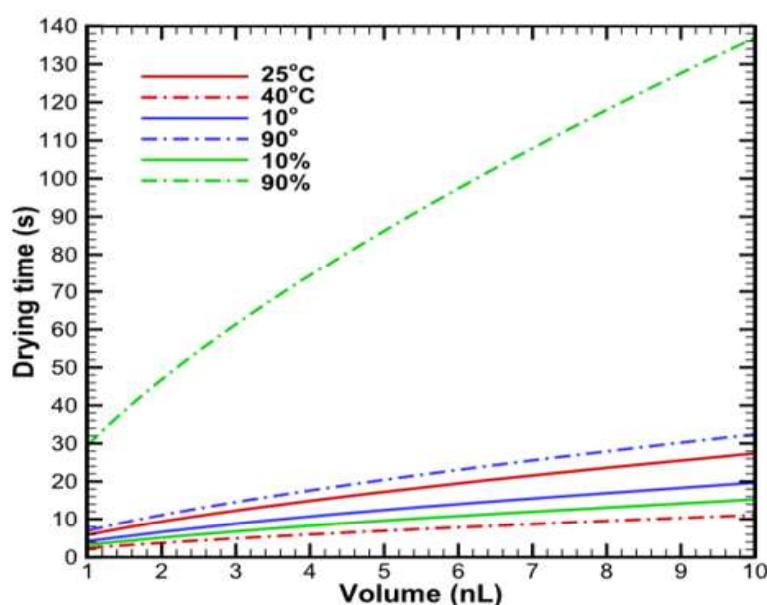

*Figure 6: Influence of droplet volume on evaporation time as a function of relative humidity, ambient temperature and surface wettability (**Source:** Physics of Fluids (2020)).*

Wettability of the droplet on solid surface evaluated by the contact angle measurement. The drop dispersion on the hydrophilic surface is higher and the loss of mass rate of liquid from the drop to the ambient is enhanced [Figure 6] i.e. the evaporation time will be reduced. The variance in temperature in several parts of the surface can reveal with the effect of the surface. A minor change in the surface

temperature can advance intensify the surface effect by manipulating the evaporation time.

Prevention of COVID-19

Controlling the spread is the most important method for prevention. The varieties in properties of the virus make it challenging namely, transmission from people with no symptoms (asymptomatic). To control the virus, some studies suggested the exposure to air (ventilation) at homes to be exposed with sunlight. Other preventable measures such as wearing a mask, even a surgical mask may be able to contain the spread together with following good hygiene during coughing in public. It is recommended that medical personnel and caretakers must wear a surgical mask during contact with the patients. It is also suggested that medical care professionals should be given, fit verified N95 respirators and shielding suits and goggles [Figure 7].
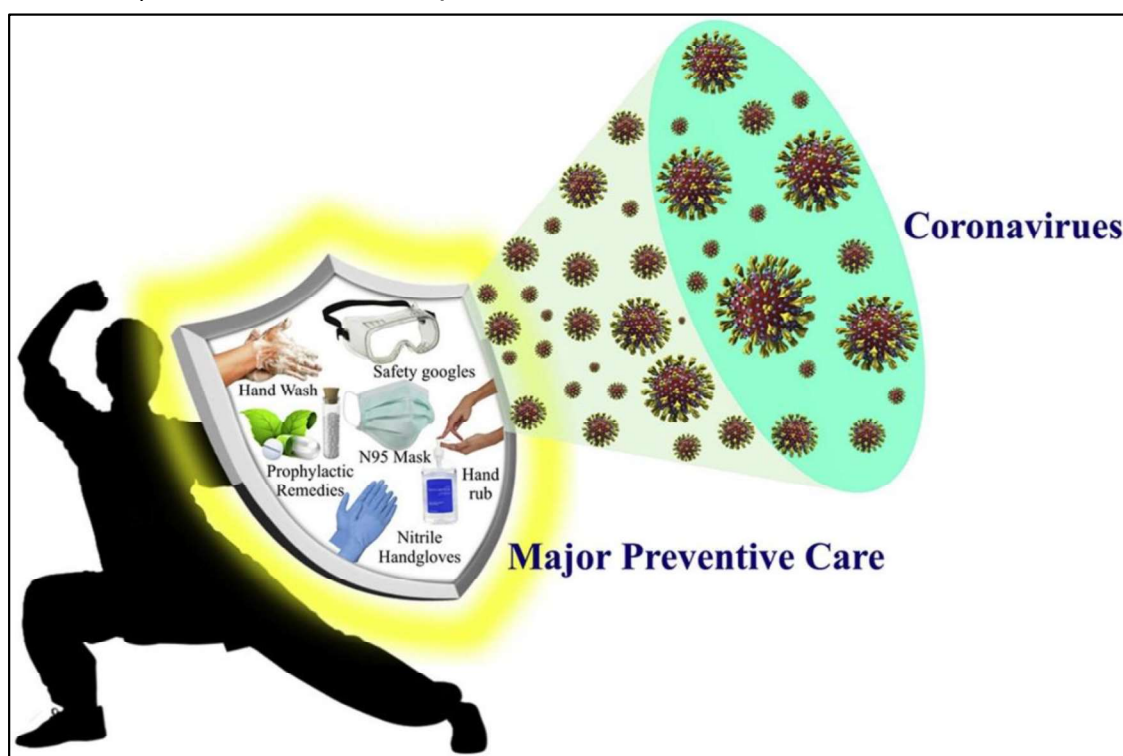
*Figure 7: Safety materials for prevention of COVID-19 (**Source:** Archives of Medical Research (2020)).*

To reduce the risk of community spread, it is recommended that people suspend unnecessary travel to areas with continuing transmission and avoid crowded areas. Good cough hygiene should be practiced by coughing in tissues/sleeves which can reduce the spread compared to coughing on the hands and practice sanitization of hands every 15–20 min periodically. Patients with respiratory symptoms are also at high risk, so they should be wearing an N95 mask or surgical masks [15].

Material Science for COVID-19: Biosafety Materials

"Biosafety material science" is a concept that has not formally been suggested up till now. Numerous studies associated to biosafety of materials (coating etc.) have already been done, including prevention, pathogen detection, control of infectious diseases and virus detection, PPE, biological invasion monitoring, salvation of human and biological resources, and defense from bioterrorism, biological weaponries [16]. Detailed studies of biosafety materials have been conducted that have advanced a broad understanding for researchers [17]. Studies have shown that the material science and engineering have wide usage in biosafety and biosafety of materials [Figure 8].

Currently, the research focus is to develop efficient materials for potential solution to the current covid-19 threats. To this end, studies have indicated that by selecting the nanoparticles with their suitable size and concentration as a filler material along with the selection of host material as well as fabrication methods can lead to the solution. Personal protection equipment or called PPE's such as shielded clothing masks, ambulance and goggles, etc. are known to provide protection against corona virus. However, because of lack of biosafety materials, these materials result in a catastrophe for the safety of numerous of health professionals as well as patients. Thus, there is an urgent need of the biosafety materials to use in current pandemic situation as well as in other applications [18].
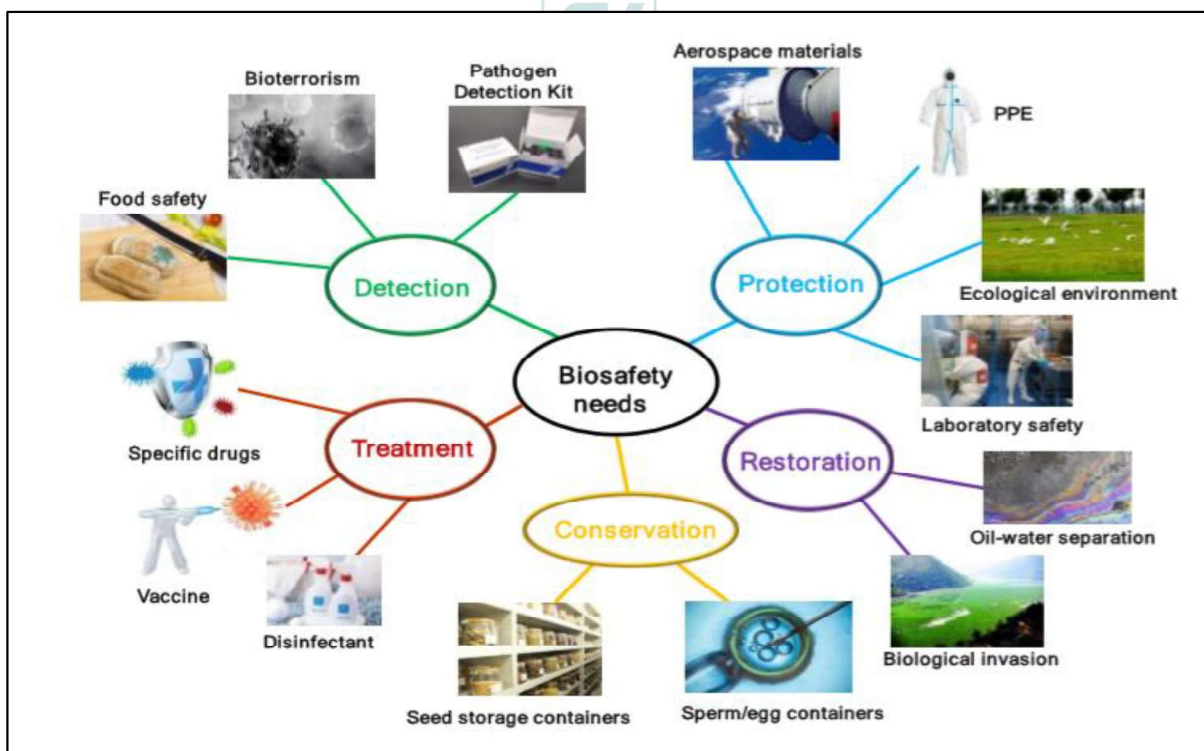
*Figure 8: Biosafety requirements and their conforming biosafety constituents (**Source:** Materials Chemistry (2020))*

Figure 8 illustrates that the material science and engineering is the best possible solution to resolve the existing challenges in the biosafety, which includes the detection, disinfection of pathogens, viral vaccines, personal protective equipment and prevention of biological species.

Viral vaccines from biosafety materials

It has been proven from the evolution virus that immunization (vaccination) is considered the only primary successful solution to totally comprehend the outbreak of virus. Vaccines efficiently contains the infection by enhancing the immunity system against a deadly pathogen. Even though many safety concerns are there in the efficiency in viral delivery system and numerous biosafety resources have been broadly studied and considered for in vivo delivery and releasing of viral vaccines comprising cationic proteins, liposomes, biological membranes and polymers. Recent researches have shown that in the form of DNA, protein or mRNA, viral vaccines can be provided. Further, all these forms can be effortlessly enzymatically tarnished when entering the blood circulation [19]. For example, in SARS-CoV-2, it contains 1273 amino acids, with a molecular weight of about 140 kDa. The DNA encoding SARS-CoV-2 would be higher than 3800 bp. To ensure the antibody available for use and assist them with being endocytosed into the cells, delivery vehicles are required. Ionizable liposomes were used to carry negatively charged mRNA for the SARSCoV- 2 spike protein by Moderna. Moreover, research shows that polymers such as low molecular-weight polyethylene mine (PEI) modified with fatty chains and poly (β-amino) esters (PABEs) can be designed to deliver DNA and mRNA. Adding to it, a cationic protein, which is natural, called as protamine with nucleic acids, can create complexes, which are negatively charged, thus being applied to provide mRNA-based therapeutics and stimulate /excite immune response [19].

Additionally, biological membranes such as RBC membranes and extracellular vesicles including macrovesicles, apoptotic bodies and exosomes can be isolated and applied for delivery of biomolecule-based vaccines. Lately, micro needle patch, an efficient drug delivery system, has appealed widespread methodical benefits due to its admirable property such as exceptional therapeutic efficiency and painless penetration. It is known to deliver a highly effective transdermal delivery method to make refined improved tools with advanced conditions for biomedical applications [20]. Altogether, it can be summarized that, biosafety materials are significant in the advancement of biomolecule-based therapeutics and it is at present applied to fight viral infection.

Conclusion

In this review, the disease outline of COVID-19 has been described as dynamic that continues. The profile of COVID 19 is evolving rapidly in the world. The zoonotic source of SARS-CoV-2 is not confirmed yet, however, sequence-based analysis has suggested bats as the key reservoir. DNA recombination was found to be involved at spike glycoprotein, which assorted SARS-CoV. Until now, no promising clinical treatments or prevention strategies have been developed against human coronaviruses. SARS had a mortality rate of 9.5%, whilst the current novel coronavirus

appears to have a mortality rate around 2%, based on the number of confirmed cases and deaths. We conclude by stressing the importance of biosafety materials in constraining COVID 19. As for the ongoing and future research, a lot of efforts are anticipated to be based on nanotechnology-based materials that are believed to provide the solution for diagnosis, prevention and the treatment of COVID-19 patients. We hope that in the near future there would be some positive information about the major role of material science in providing biosafety solution.

References:

1. C. Wang, P.W. Horby, F.G. Hayden, G.F. Gao, A novel coronavirus outbreak of global health concern, Lancet. 395 (2020) 470–473, DOI:https://doi.org/10.1016/S0140-6736(20)30185-9

2. A. Wu, Y. Peng, B. Huang, X. Ding, X. Wang, P. Niu, J. Meng, Z. Zhu, Z. Zhang, J. Wang, J. Sheng, L. Quan, Z. Xia, W. Tan, G. Cheng, T. Jiang, Genome Composition and Divergence of the Novel Coronavirus (2019-nCoV) Originating in China, Cell Host Microbe. 27 (2020) 325–328, DOI:https://doi.org/10.1016/j.chom.2020.02.001

3. X. Ma, D. Ph, D. Wang, D. Ph, W. Xu, G. Wu, G.F. Gao, D. Phil, W. Tan, D. Ph, A Novel Coronavirus from Patients with Pneumonia in China, 2019, (2020) 1–7, DOI:10.1056/NEJMoa2001017

4. D. Kumar, Corona Virus: A Review of COVID-19, Eurasian J. Med. Oncol. 4 (2020) 8–25, DOI:10.14744/ejmo.2020.51418

5. T. Singhal, A Review of Coronavirus Disease-2019 (COVID-19), Indian J. Pediatr. 87 (2020) 281–286, DOI: https://doi.org/10.1007/s12098-020-03263-6

6. C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, L. Zhang, G. Fan, J. Xu, X. Gu, Z. Cheng, T. Yu, J. Xia, Y. Wei, W. Wu, X. Xie, W. Yin, H. Li, M. Liu, Y. Xiao, H. Gao, L. Guo, J. Xie, G. Wang, R. Jiang, Z. Gao, Q. Jin, J. Wang, B. Cao, Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, Lancet. 395 (2020) 497–506, DOI: DOI:https://doi.org/10.1016/S0140-6736(20)30183-5

7. C. Rothe, M. Schunk, P. Sothmann, G. Bretzel, G. Froeschl, C. Wallrauch, T. Zimmer, V. Thiel, C. Janke, W. Guggemos, M. Seilmaier, C. Drosten, P. Vollmar, K. Zwirglmaier, S. Zange, R. Wölfel, M. Hoelscher, Transmission of 2019-NCOV infection from an asymptomatic contact in Germany, N. Engl. J. Med. 382 (2020) 970–971, DOI: 10.1056/NEJMc2001468

8. L. Zhou, M. Med, Y. Tong, D. Ph, R. Ren, M. Med, Q. Chen, M. Sc, D. Li, T. Liu, B. Med, J. Zhao, M. Sc, M. Li, M. Sc, W. Tu, M. Med, C. Chen, M. Sc, L. Jin, M. Med, R. Yang, M. Med, Q. Wang, S. Zhou, M. Med, R. Wang, Z. Deng, M. Med, B. Liu, Z. Ma, M. Med, B. Yang, M. Sc, G.M. Leung, Z. Feng, M. Med, Early Transmission Dynamics in Wuhan, China, of Novel

Coronavirus–Infected Pneumonia, (2020) 1–9, DOI: 10.1056/NEJMoa2001316

9. Y. Yin, R.G. Wunderink, MERS, SARS and other coronaviruses as causes of pneumonia, Respirology. 23 (2018) 130–137, DOI: https://doi.org/10.1111/resp.13196

10. P.D. Thomas G. Ksiazek, D.V.M., Ph.D., Dean Erdman, Dr.P.H., Cynthia S. Goldsmith, M.S., Sherif R. Zaki, M.D., M.P.H. Teresa Peret, Ph.D., Shannon Emery, B.S., Suxiang Tong, Ph.D., Carlo Urbani, M.D.,* James A. Comer, Ph.D., P.D. Wilina Lim, M.D., Pierre E. Rollin, M.D., Scott F. Dowell, M.D., M.P.H., Ai-Ee Ling, M.D., Charles D. Humphrey, P.D. Wun-Ju Shieh, M.D., Ph.D., Jeannette Guarner, M.D., Christopher D. Paddock, M.D., M.P.H.T.M., Paul Rota, M.D. Barry Fields, Ph.D., Joseph DeRisi, Ph.D., Jyh-Yuan Yang, Ph.D., Nancy Cox, Ph.D., James M. Hughes, and the S.W.G. James W. LeDuc, Ph.D., William J. Bellini, Ph.D., Larry J. Anderson, M.D., A Novel Coronavirus Associated with Severe Acute Respiratory Syndrome Thomas, N. Engl. J. Med. 348 (2020) 1953–1966, DOI: https://doi.org/10.1093/jtm/taaa008

11. L.E. Gralinski, V.D. Menachery, Return of of the Coronavirus: Viruses. 12 (2020) 1–8, DOI: https://doi.org/10.3390/v12020135

12. Leslie Dietz, Patrick F. Horve, David A. Coil, Mark Fretz, Jonathan A. Eisen, Kevin Van Den Wymelenberg, 2019 Novel Coronavirus (COVID-19) Pandemic: Built Environment Considerations To Reduce Transmission, mSystems, 2020, 5 Issue 2 e00245-20, https://doi.org/10.1128/mSystems.00245-20

13. R. Bhardwaj, A. Agrawal, Likelihood of survival of coronavirus in a respiratory droplet deposited on a solid surface Likelihood of survival of coronavirus in a respiratory droplet deposited on a solid surface, 061704 (2020), DOI: https://doi.org/10.1063/5.0012009

14. D. Chang, H. Xu, A. Rebaza, L. Sharma, C.S. Dela Cruz, Protecting health-care workers from subclinical coronavirus infection, Lancet Respir. Med. 8 (2020) e13, DOI: https://doi.org/10.1016/S2213-2600(20)30066-7

15. J. Li, J. (Justin) Li, X. Xie, X. Cai, J. Huang, X. Tian, H. Zhu, Game consumption and the 2019 novel coronavirus, Lancet Infect. Dis. 20 (2020) 275–276, DOI: https://doi.org/10.1016/S1473-3099(20)30063-3

16. Q. Li, Y. Wu, H. Lu, X. Wu, S. Chen, N. Song, Y.W. Yang, H. Gao, Construction of Supramolecular Nanoassembly for Responsive Bacterial Elimination and Effective Bacterial Detection, ACS Appl. Mater. Interfaces. 9 (2017) 10180–10189, DOI: 10.1021/acsami.7b00873

17. A. Manuscript, MATERIALS CHEMISTRY, (2020), DOI: https://doi.org/10.1039/D0QM00255K

18. S.P. Sullivan, D.G. Koutsonanos, M. Del Pilar Martin, J.W. Lee, V. Zarnitsyn, S.O. Choi, N. Murthy, R.W. Compans, I. Skountzou, M.R. Prausnitz, Dissolving polymer microneedle patches for influenza vaccination, Nat. Med. 16

(2010)   915–920,   DOI:
https://doi.org/10.1038/nm.2182

19. V. Ricotta, Y. Yu, N. Clayton, Y.C. Chuang, Y. Wang, S. Mueller, K. Levon, M. Simon, M. Rafailovich, A chip-based potentiometric sensor for a Zika virus diagnostic using 3D surface molecular imprinting, Analyst. 144 (2019) 4266–4280,   DOI:
https://doi.org/10.1039/C9AN00580C