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A Review of SARS-CoV-2 Vaccine Developmental Stages and Immunization Challenges

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Abstract

The SARS-CoV-2 virus has been spreading rapidly within the range of infected patients, with an alarming fatality rate, so it has become a global pandemic and public health concern. As a result of this situation, an accelerated track for vaccine development has been set in motion. A vaccine, which is made from biological products, would be the ultimate weapon against the coronavirus and the best way to return to normal life. Several SARS-CoV-2 vaccine candidates have been identified in preclinical models and are currently being tested in clinical trials. SARS and the virus that causes Covid-19, SARS-CoV-2, are nearly identical, and both use spike proteins to bind to a specific receptor found on cells in human lungs. Based on previous involvement in the development of SARS-CoV vaccines, the SARS-CoV-2 immunization is currently being developed instantly in a variety of ways. Shortcuts in any of the steps of the research and development process can result in significant health hazards as well as a decrease in social confidence in the benefits of a vaccine. The purpose of this comprehensive review was to represent the developmental stages and challenges of various vaccine varieties used in the COVID-19 disorder.

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Introduction

Coronavirus disease 2019 (COVID-19) is an illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; formerly known as 2019-nCoV), a novel coronavirus found during a respiratory sickness outbreak in Wuhan, China. This new virus has a high infectivity and is capable of spreading to people. On March 11, 2020, the World Health Organization declared a COVID-19 pandemic after establishing that the disease had spread globally.[1] Corona, which means "crown" in Latin, is a single-stranded, positive-sense RNA virus with the second-largest genome. The spike (S), membrane (M), and envelope (E) proteins, which are all embedded inside the microbial surface envelope, and the nucleocapsid (N) protein, which is in the ribonucleoprotein core, are the four key structural proteins found in this virus.[2]

The angiotensin-converting enzyme 2 receptor is abundant on the apical region of alveolar epithelial cells, alveolar monocytes and macrophages in the lungs (consistent with the first injury in the distal airway), small intestine enterocytes, vascular epithelial tissue cells, heart, and kidneys, which are the common target organs involved in SARS-CoV-2 pathogenesis.[3] Bats SL-CoVZXC21 and bat-SL-CoVZC45 are thought to share 90% of SARS-DNA COV-2's.

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This finding suggested the possibility that mammals are the link between SARS-COV-2 and humans.[4] Primary efforts to reduce COVID-19 damage focus on confinement, with physical distance and several infection-prevention strategies. The most pressing problem at this time is to find a means to interrupt the transmission channels and stop the infection from spreading.[5] The majority of COVID-19 potential vaccines based on infectious agent antigens or gene sequences aim to produce neutralizing antibodies against the organism's spike protein (S), which prevents uptake via the human ACE2 receptor and hence prevents infection.[6]

Various types of vaccine development:

The vaccine is a synthetic biological product that confers active immunity to a particular infectious illness. Both innate and acquired immunological activation are involved in the immune response to SARS-CoV-2.[7] The majority of viral infections are protected by virus-neutralizing antibodies, a principle that is true for the vast majority of viral infections. Humans develop powerful immune protection as a result of infection or vaccination.[8] The S proteins of SARS-CoV and SARS-CoV-2 bind to angiotensin-converting enzyme 2 (ACE2), however the S protein of MERS-CoV binds to dipeptidyl peptidase-4 (DPP4). In preclinical models, several S protein-based vaccines against SARS-CoV and MERS-CoV have been demonstrated to generate powerful immune responses and protective benefits.[9] However, only a few of them were chosen for clinical trials and these approaches hold different types of vaccines.[10]

Phases of clinical trials:

The average time it takes to produce a vaccine is 12-15 years. Clinical trials to show the efficacy of a vaccination target, which represents its potential to prevent disease, with minimal adverse responses in short-term studies.[11] Over 280 different COVID-19 vaccines are being developed at various levels. Some are made with currently available vaccination technology, while others are made with completely new methodologies. Although clinical trials are completed faster than they are for other vaccines, this was accomplished by doing a number of stages in simultaneously rather than sequentially, and vaccine safety was not compromised.[12] If the pre-clinical phase yields promising results, vaccination candidates are tested in three clinical trial phases to determine whether they are safe and efficacious in humans.[13]

The first phase is testing proposed vaccines on a small group of healthy persons (20–80) in order to ensure that they are safe and effective. A dose step-up experiment, in which groups of participants are given rising amounts of the immunogen, is also used to identify the optimum dose. Candidate vaccines will proceed to phase II if phase I results are positive. The second phase includes testing the immunogen on a larger sample size (100–300) and is expected to provide therapeutically useful data on the candidate vaccine's safety, immunogenicity, and effectiveness. Before moving on to phase III, it may be essential to undertake many phase II studies to deal with schedules, age group variances, and follow-up duration.[14] The most important part of a study on which licensing is based in Phase III. The vaccine is given to a large number of people (1000–3000) in the target population during this phase. A single study may not be sufficient to address all questions, thus the vaccine should be tested under a variety of situations, including disease patterns and

populations. If the phase III results show that the vaccine is efficacious and safe, the manufacturer will apply to a national regulatory authority for a license to market it.[15]

Covid vaccine:

Because COVID 19 infection is the key concern, most vaccine candidates in clinical trials target the coronavirus spike protein and its variations.[16] Supermolecule technologies (nucleoside-modified ribonucleic acid and DNA), non-replicating infective agent vectors, peptides, recombinant proteins, live attenuated viruses, and inactivated viruses were among the platforms being developed in 2020.[17] An RNA vaccine contains ribonucleic acid that, when introduced into a tissue, acts as messenger RNA (mRNA) to cause cells to produce the foreign protein and trigger an adaptive immune response that instructs the body on how to establish and destroy the corresponding microorganism or cancer cells. RNA vaccines were the first COVID-19 vaccines to be approved in the United States and, as a result, by the World Organization. The Pfizer-BioNTech COVID 19 vaccine, and hence the Moderna COVID-19 vaccine, are the only licensed vaccines of this type as of January 2021.[18] Adenovirus vector vaccines are non-replicating viral vectors that use an adenovirus shell carrying DNA to transfer genetic code for an antigen that encodes a SARS-CoV-2 macromolecule. Infectious agents do not produce new virus particles; instead, they produce just the component that causes a broad immune response.[19] Unlike most traditional vaccinations, viral vector-based vaccines do not include antigens; instead, they rely on the body's own cells to provide them. Inactivated viral vaccines contain virus particles that have been completely developed in culture and then killed using a technology such as heat or formaldehyde to lose their disease-producing capacity while still eliciting an immune response.[20] Because of the Indian Covaxin, the Chinese CoronaVac and BBIBP-CorV vaccines were licensed in January 2021. Subunit vaccinations provide one or more antigens while avoiding the introduction of complete infective agent particles.[21] The peptide vaccination EpiVacCorona is the only licensed immunizing product of this class as of January 2021.

Bangladesh situation:

Bangladesh started administering COVID-19 vaccinations on January 27, 2021, and mass vaccination on February 7, 2021.[22] On November 5, 2020, the Bangladeshi government, India's Serum Institute, and Bangladesh's Beximco Pharma signed a tripartite agreement & Bangladesh ordered 30 million doses of Oxford–AstraZeneca COVISHIELDTM Vaccine (ChAdOx1-S) for emergency use from Serum through Beximco for $4 per shot under the agreement.[23] Despite the fact that Bangladesh paid for it, India fails to deliver half of the agreed-upon doses on schedule. Bangladesh licensed Russian Sputnik V and Chinese BBIBP-CorV vaccines for emergency use in late April 2021, following a vaccination scarcity.[22]

COVID-19 Vaccine Challenges:

To obtain the best effects, a vaccination must overcome a number of obstacles. The following are the details:

Effectiveness-

In the instance of COVID 19, a vaccine efficacy of 67% may be sufficient to halt the pandemic. This, however, presupposes that the vaccine provides sterilizing immunity, which is important for preventing transmission.[24] Because of the

effectiveness required to authorize a COVID 19 vaccine, the FDA and the EMA set a 50 percent limit. Efficacies for the Oxford–AstraZeneca vaccine (different dose regimens) range from 62–90% to 95 percent for the Pfizer-BioNTech COVID 19 vaccine. In the United Arab Emirates, Sinopharm announced that a vaccination was 86 percent effective. For people aged 18 to 64, the Moderna COVID-19 vaccine has a 96 percent efficacy rate. In the United Kingdom, the Novavax vaccine was shown to be 89% effective.[25]

Protection from Coronavirus variants-

As the virus spreads, little changes or mutations occur, resulting in new virus variants & winning variants will become dominant. They have a significant mutation known as E484K, which allows the virus to bypass immune system components known as antibodies, which may battle coronavirus-supported expertise from past infection or a vaccine.[26] Every one of those variants has a slightly different genetic code. Variant's virus is causing an increase in new infected cases over the world. The effectiveness of the Pfizer/BioNTech and Moderna mRNA vaccines against mutations discovered in the B.1.1.7 and B.1.351 variants was investigated in lab tests. The vaccination, on the other hand, was ineffective against virus-containing mutations observed in the B.1.351 strain.

Long-Term Immunity-

Various studies on the coronavirus family, including severe acute respiratory syndrome(SARS) and Middle East Respiratory Syndrome (MERS), as well as an early study on SARS-CoV-2, have suggested that infection does not confer long-term protection. Antibodies and memory B- and T-cells were discovered in recovered COVID- 19 patients for up to 3 months, according to a recent study.[27] Even if long-term immunity isn't achieved, a vaccine can safeguard susceptible people and health-care workers by lowering the amount of virus that a vaccinated person generates and transmits.[28]

Antibody-Dependent Enhancement (ADE) of the disease-

Antibody-mediated protection is well-represented, and antibody detection is used to evaluate the efficacy of the different human vaccines. Antibodies, on the other hand, may boost inflammatory responses, based on previous experience with other viruses. Because of the existence of poorly neutralizing cross-reactive antibodies that bind to the virus and accelerate microorganism entrance into cells, this is known as antibody-dependent enhancement (ADE).[29] Low immunological gamma globulin (IgG) antibody levels in transfused plasma were linked to higher mortality, and when plasma Ig levels increased, mortality reduced.[30]

Worldwide Distribution-

The SARS-CoV-2 vaccine is now available on the market, and it will be necessary to manufacture and distribute enough vaccine to immunize the entire world's population.[31] The World Health Organization (WHO) has warned that economic policies may hamper international accessibility, which can have devastating consequences for low- and middle-income countries (LMICs).[32] The cost of the COVID-19 vaccines has also been questioned. According to reports, there may be a wide range of rates across countries, with poorer, smaller countries and people with little purchasing power paying the most.[33]

Selection of COVID-19 Vaccine receiver-

When the COVID-19 vaccine supply is restricted, individual countries will receive the first doses based entirely on their population, and

governments will decide how to distribute the vaccine. Healthcare workers, from physicians to medical students, hospital maintenance staff to domestic aides, and others, as well as people who live in long-term care facilities, such as nursing homes and assisted living facilities, are a priority because older adults are more likely to require hospitalization or death as a result of Covid-19.[34]

Vaccine Hesitancy-

Vaccine hesitancy is a major barrier to a vaccine program's success. People who oppose vaccines believe that if a person has the illness naturally and recovers, the immune system's response to the virus will be greater. Others believe that vaccines are not thoroughly studied and monitored prior to their approval.[35] It's necessary to reach out to these people, because trust is crucial if SARS-CoV-2 immunizations are to be effective. In contrast to the preceding, numerous members of the World Health Organization have personally experienced the pandemic's effects and are eagerly awaiting vaccination once a vaccine becomes available.[36]

Conclusion

COVID-19 vaccinations that are both safe and effective are a critical step toward allowing us to do more of the things we love with the people we care about. Despite efforts to produce a vaccine for SARS-CoV-2, experts warn that a vaccine will not completely eradicate the disease since levels of effectiveness may vary or be partial, and not everyone can or wants to be vaccinated. The numerous ranges of examined technical platforms are a significant aspect within the landscape of SARS-CoV-2 vaccine research and development. We hope to implement this critical tool for disease prevention as soon as possible.

References

1. *World Health Organization, WHO Announces COVID-19 Outbreak a Pandemic, [Online] Available at: http://www.euro.who.int/en/ heps//: coronavirus.jhu.edu/ map.alth-topics/ health-emergencies/coronavirus-covid-19/ news/ news/2020/3/who-announces-covid-19 outbreak -a-pandemic (Accessed 1 March 2021).*

2. *Dai L, Gao GF. Viral targets for vaccines against COVID-19. Nat Rev Immunol. 2021 Feb;21(2):73-82. doi: 10.1038/s41577-020-00480-0.*

3. *Bennet BM, Wolf J, Laureano R, Sellers RS. Review of Current Vaccine Development Strategies to Prevent Coronavirus Disease 2019 (COVID-19). Toxicol Pathol. 2020 Oct;48(7):800-809.doi: 10.1177/0192623320959090.*

4. *Alturki SO, Alturki SO, Connors J, Cusimano G, Kutzler MA, Izmirly AM, Haddad EK. The 2020 Pandemic: Current SARS-CoV-2 Vaccine Development. Front Immunol. 2020 Aug 19;11:1880. doi: 10.3389/fimmu.2020.01880.*

5. *COVID-19 the Essentials of Prevention and Treatment JIE-MING QU, Publisher: Glyn Jones, COVID-19 © 2021 Shanghai Jiao Tong University Press. Published by Elsevier Inc. https://doi.org/10.1016/B978-0-12-824 003 - 8.00001-2A.*

6. *Kyriakidis NC, López-Cortés A, González EV, Grimaldos AB, Prado EO. SARS-CoV-2 vaccines strategies: a comprehensive review of phase 3 candidates. NPJ Vaccines. 2021 Feb 22;6(1):28. doi: 10.1038/s41541-021-00292-w.*

7. *Speiser DE, Bachmann MF. COVID-19: Mechanisms of Vaccination and Immunity. Vaccines (Basel). 2020 Jul 22;8(3):404. doi: 10.3390/vaccines8030404.*

8. *Strizova Z, Smetanova J, Bartunkova J, Milota T. Principles and Challenges in anti-COVID-19 Vaccine Development. Int Arch Allergy Immunol. 2021;182(4):339-349. doi: 10.1159/000514225.*

9. *Ni W, Yang X, Yang D, Bao J, Li R, Xiao Y, Hou C, Wang H, Liu J, Yang D, Xu Y, Cao Z, Gao Z. Role of angiotensin-converting enzyme 2 (ACE2) in COVID-19. Crit Care. 2020 Jul 13;24(1):422. doi: 10.1186/s13054-020-03120-0.*

10. *The different types of COVID-19 vaccines, www.who.int › Newsroom › Feature stories › Detail Jan 12, 2021.*

11. *Dagotto G, Yu J, Barouch DH. Approaches and Challenges in SARS-CoV-2 Vaccine Development. Cell Host Microbe. 2020 Sep 9;28(3):364-370. doi: 10.1016/j.chom.2020.08.002.*

12. *Fossaluza V, Diniz JB, Pereira Bde B, Miguel EC, Pereira CA. Sequential allocation to balance prognostic factors in a psychiatric clinical trial. Clinics (Sao Paulo). 2009;64(6):511-8. doi: 10.1590/s1807-59322009000600005.*

13. *Pronker ES, Weenen TC, Commandeur H, Claassen EH, Osterhaus AD. Risk in vaccine research and development quantified. PLoS One.2013;8(3):e57755.doi:10.1371/journal. Pon e.0057755.*

14. *Di Pasquale A, Bonanni P, Garçon N, Stanberry LR, El-Hodhod M, Tavares Da Silva F. Vaccine safety evaluation: Practical aspects in assessing benefits and risks. Vaccine. 2016. Dec20;34(52):6672-6680.doi:10.1016/j.vaccine. 2016.10.039.*

15. *Mellet J, Pepper MS. A COVID-19 Vaccine: Big Strides Come with Big Challenges. Vaccines (Basel). 2021 Jan 11;9(1):39.*

16. *Krammer F. SARS-CoV-2 vaccines in development. Nature. 2020 Oct; 586 (7830): 516-527. doi: 10.1038/s41586 -020-2798-3.*

17. *Ng WH, Liu X, Mahalingam S. Development of vaccines for SARS-CoV-2. F1000Res. 2020 Aug 17;9:F1000 Faculty Rev-991. doi: 10.12688/f1000research.25998.1.*

18. *World Health Organization. (2020). mRNA vaccines against COVID-19: Pfizer-BioNTech COVID-19 vaccine BNT162b2: prepared by the Strategic Advisory Group of Experts (SAGE) on immunization working group on COVID-19 vaccines, 22 December 2020.*

19. *What is viral vector-based vaccines and how could they be used against COVID- 19? Available at https://www.gavi.org/vaccines work/what-are-viral-vector-based-vaccines-and-how-could-they-be-used-against-covid-19).*

20. *Sanders B, Koldijk M, & Schuitemaker H. Inactivated Viral Vaccines. Vaccine Analysis: Strategies, Principles, and Control.2014 Nov 28:45–80. https://doi.org/10.1007/978-3-662-45024-6_2.*

21. *Mahlen SD, Koneman EW, Papasian CJ, & Selvarangan R. Medical microbiology and immunology. In Pathology Exam Review. 2012:225–282. Wolters Kluwer Health. https://doi.org/10.1093/lab med/24.8.531.*

22. *Nurunnabi ASM, Ashique SS, Jahan A, Sweety AA, Sharmin S. Children and COVID-19 Vaccine: A Public Health Ethics Perspective. Bangladesh Med J. 2021;50(3):44-8. https://doi.org/10.3329/bmj.v50i3.62934.*

23. *Oxford University-Astrazeneca vaccine: Bangladesh okays it for emergency use". The Daily Star. 4 January 2021. Retrieved 7 January 2021, Oxford University-Astrazeneca vaccine: Bangladesh okays it for emergency use | The Daily Star.*

24. *Lin C, Tu P, Beitsch LM. Confidence and Receptivity for COVID-19 Vaccines: A Rapid Systematic Review. Vaccines (Basel). 2020 Dec 30;9(1):16. doi: 10.3390/ vaccines9010016.*

25. *COVID-19 vaccines - WHO | World Health Organization, https://www.who.int/.../covid-19-vaccines.*

26. *Covishield, Covaxin effective against 'Indian strain' of coronavirus, study suggests, Accessed on 27/4/2021 Available at https://www.newindianexpress.com/nation/2021 /apr/...).*

27. *Rodda LB, Netland J, Shehata L, Pruner KB, Morawski PA, Thouvenel CD, Takehara KK, Eggenberger J, Hemann EA, Waterman HR, Fahning ML, Chen Y, Hale M, Rathe J, Stokes C, Wrenn S, Fiala B, Carter L, Hamerman JA, King NP, Gale M Jr, Campbell DJ, Rawlings DJ, Pepper M. Functional SARS-CoV-2-Specific Immune Memory Persists after Mild COVID-19. Cell. 2021 Jan 7;184(1):169-183.e17. doi: 10.1016/j.cell.2020.11.029.*

28. *Stat News,The World Needs Covid-19 Vaccines. It May Also be Overestimating Their Power. [(accessed on 5 March 2021)]; Available online: https://www.statnews.com /2020/05/22/the-world-needs-covid-19-vaccines-it-may-also-be-overestimating-their-power/.*

29. *Yang L, Liu S, Liu J, Zhang Z, Wan X, Huang B, Chen Y, Zhang Y. COVID-19: immunopathogenesis and Immunotherapeutics. Signal Transduct Target Ther. 2020 Jul 25;5(1):128. doi: 10.1038/s41392-020-00243-2.*

30. *Joyner MJ, Carter RE, Senefeld JW, Klassen SA, Mills JR, Johnson PW, Theel ES, Wiggins CC, Bruno KA, Klompas AM, Lesser ER, Kunze KL, Sexton MA, Diaz Soto JC, Baker SE, Shepherd JRA, van Helmond N, Verdun NC, Marks P, van Buskirk CM, Winters JL, Stubbs JR, Rea RF, Hodge DO, Herasevich V, Whelan ER, Clayburn AJ, Larson KF, Ripoll JG, Andersen KJ, Buras MR, Vogt MNP, Dennis JJ, Regimbal RJ, Bauer PR, Blair JE, Paneth NS, Fairweather D, Wright RS, Casadevall A. Convalescent Plasma Antibody Levels and the Risk of Death from Covid-19. N Engl J Med. 2021 Mar 18;384(11):1015-1027. doi: 10.1056/NEJMoa2031893.*

31. *Hodgson SH, Mansatta K, Mallett G, Harris V, Emary KRW, Pollard AJ. What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2. Lancet Infect Dis. 2021 Feb;21(2):e26-e35. doi: 10.1016/S1473-3099(20)30773-8.*

32. *Dzinamarira T, Dzobo M, Chitungo I. COVID-19: A perspective on Africa's capacity and response. J Med Virol. 2020 Nov;92(11):2465-2472. doi: 10.1002/jmv. 26159.*

33. *Forman R, Shah S, Jeurissen P, Jit M, Mossialos E. COVID-19 vaccine challenges: What have we learned so far and what remains to be done? Health Policy. 2021 May;125(5):553-567. doi: 10.1016/j.healthpol. 2021.03.013.*

34. *Readiness, C. (2021). Monitoring COVID-19 vaccination.https://www.who.int/initiatives/act-accelerator/covax/covid-19-vaccine-country-readiness-and-delivery.*

35. *DeFrancesco L. Whither COVID-19 vaccines? Nat Biotechnol. 2020 Oct;38(10):1132-1145. doi: 10.1038/s41587-020-0697-7.*

36. *Reno C, Maietti E, Fantini MP, Savoia E, Manzoli L, Montalti M, Gori D. Enhancing COVID-19 Vaccines Acceptance: Results from a Survey on Vaccine Hesitancy in Northern Italy. Vaccines (Basel). 2021 Apr 13;9(4):378. doi: 10.3390/vaccines9040378.*