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**COVID-19: IMPACT ON HUMAN HEALTH**

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**ABSTRACT**

Researchers are on the cutting edge of devising the best strategy to combat the SARS-CoV-2 pandemic by studying and exploring the pathogenesis, prevention, and treatment as the world continues to be plagued by an increasing number of confirmed COVID-19 cases. The primary method for detecting the virus is via antigen testing and more accurate molecular tests such as rt PCR using patient samples. The most prevalent treatments for COVID-19 infection include steroidal drugs, monoclonal antibodies therapy and remdesivir an anti-viral drug. Despite the fact that these medicines exist and are widely utilised in hospitals all over the world, professionals frequently question their efficacy and usefulness in patients. Furthermore, most targeted therapeutics aim is to disrupt or reduce the interaction of SARS COV-2 spike protein and host cell receptors. In addition to treatment, the most effective technique of stopping the spread of COVID-19 is the development and use of various vaccines candidates which are showing promising results in preventing severe symptoms of the virus. Therefore, more research on COVID-19 pathophysiology, clinical implications, identification (different mutants), diagnosis, and treatment is required, which will help world to overcome this pandemic.

**Keywords:** COVID-19, SARS-CoV-2, Vaccines candidates, Spike Protein, Treatment

**INTRODUCTION**

SARS-CoV-2 is a coronavirus that can infect humans and cause COVID-19 disease. Although most people can recover from its mild symptoms, on the other hand it can cause serious illness in older individuals. By avoid touching other peoples and always sanitizing and washing your hands before eating and drinking and always wearing a mask while travelling out and also by keeping a safe distance from the infected persons. The virus mainly spreads through secretions/droplets from the nose by inhaling droplets of saliva or by sneezing. Viral infection can be spread by sneezing or coughing from an infected person to a healthy one. The particles can be inhaled by the healthy person through the nose, eyes or mouth.

Among the types Beta, delta, alpha and gamma are the four genera of coronaviruses **[**[**1**](http://scholar.google.com/scholar_lookup?hl=en&publication_year=2015&pages=1-23&author=AR+Fehr&author=S+Perlman&title=Coronaviruses%3A+An+Overview+of+their+Replication+and+Pathogenesis%2C+in+Coronaviruses)**].** Previous diseases such as SARS and MERS were also coronavirus infections **[**[**2**](http://scholar.google.com/scholar?hl=en&q=+WHO.+Naming+the+coronavirus+disease+%28COVID%E2%80%9019%29+and+the+virus+that+causes+it.+https%3A%2F%2Fwww.who.int%2Femergencies%2Fdiseases%2Fnovel-coronavirus-2019%2Ftechnical-guidance%2Fnaming-the-coronavirus-disease-%28covid-2019%29-and-the-virus-that-causes-it+%28accessed+25+August+2020%29.)**].** COVID-19 is highly infectious and transmissible virus. It has caused outbreaks in over 200 countries**.[****3-****6]** The virus has been known to cause various respiratory conditions such as pneumonia and severe hypothermia.**[**[**7**](http://scholar.google.com/scholar?hl=en&q=+WHO.+COVID%E2%80%9019+weekly+epidemiological+update.+https%3A%2F%2Fwww.who.int%2Fdocs%2Fdefault-source%2Fcoronaviruse%2Fsituation-reports%2F20201110-weekly-epi-update-13.pdf%3Fsfvrsn%3D24435477_15%26download%3Dtrue+%28accessed+10+November+2020%29.)**]** The proportion of male and female patients did not differ significantly, and infection in youngsters was uncommon, contrary to the findings of a prior study by Zhong et al. **[22]**

As per WHO in India there are approximately 47 million confirmed cases reported and globally 396 million cases reported till date. **[20]**

The primary symptoms were cough and fever, which matched Zhao et al findings. **[22]** Other symptoms included myalgia, tiredness, dyspnea, and anorexia. Intestinal signs and symptoms (e.g., diarrhoea) were uncommon in COVID-19 patients, but diarrhoea was reported in roughly 20% to 25% patients. [**23]** ARDS, arrhythmia, and shock were the most common complications during hospitalisation. Patchy spot shadows of the bilateral lungs and also a ground glass shadow were observed all the COVID-19 CT scan many patients were over 60 and had more fundamental disorders compare to the adults.

 According to the analysis, the vast majority of confirmed cases, had imaging of typical pulmonary changes. Lung abnormalities like pleomorphic, intestitial change, ground glass and patchy shadows were induced by COVID-19. The patient's symptoms and the findings of nucleic acid testing were frequently out of sync with the imaging of lung abnormalities.

**ORIGIN OF SARS-COV-2**

It has been previously reported that coronaviruses are derived from bats.**[**[**8**](http://scholar.google.com/scholar_lookup?hl=en&volume=310&publication_year=2005&pages=676-679&journal=Science&author=W+Li&author=Z+Shi&author=M+Yu&author=W+Ren&author=C+Smith&author=JH+Epstein&title=Bats+are+natural+reservoirs+of+SARS%E2%80%90like+coronaviruses)**]** The sequencing of SARS-CoV-2 revealed that it is more than 80% similar to SARS-CoV and more than 50% similar to MERS-CoV. Spike of SARS CoV-2 protein has been found to be identical to that of a virus found in pangolins**.[9]** The first COVID-19 case was reported in December 2019 in Wuhan, China, a city in the Hubei province. [[**10**](http://scholar.google.com/scholar_lookup?hl=en&volume=7&publication_year=2020&pages=1012-1023&journal=Natl+Sci+Rev&author=X+Tang&author=C+Wu&author=X+Li&author=Y+Song&author=X+Yao&author=X+Wu&title=On+the+origin+and+continuing+evolution+of+SARS%E2%80%90CoV%E2%80%902)**]** The genomic sequences of SARS-CoV-2 isolated from many patients shared a sequence identity greater than 99.9%, indicating a recent host shift from nature to humans. According to the phylogenetic tree constructed in the study, SARS-CoV-2 was closest to RaTG13 (bat coronavirus), followed by GD Pangolin SARSr-CoV, and finally human SARS-CoV**. [**[**10**](http://scholar.google.com/scholar_lookup?hl=en&volume=7&publication_year=2020&pages=1012-1023&journal=Natl+Sci+Rev&author=X+Tang&author=C+Wu&author=X+Li&author=Y+Song&author=X+Yao&author=X+Wu&title=On+the+origin+and+continuing+evolution+of+SARS%E2%80%90CoV%E2%80%902)**]**

**Immunological reponses**

Macrophages serve as first-line antigen-presenting cells, producing cytokines such as interleukin (IL)-12, IL-15, and IL-18 in response to virus antigen recognition. Natural killer cells bind to show their activation and chemical reaction as well as differentiation of helper T cells. There is increased expression of cytokines such as interferon, tumor necrosis factor, interleukin, as well as activation of natural killer cells, which secrete perforin, granzymes, reactive oxygen species, nitric oxide, and cytotoxic T lymphocytes to kill the virus. **[35]**

**DETECTION OF CORONAVIRUS**

Reverse Transcription polymerase chain reaction (rtPCR) was used to detect all suspected cases. Virus was isolated from samples from nasal swab and from the patients throats and its RNA is extracted and converted into DNA, after that amplification is done **[11]**

The spread of virus take place in the form of minute liquid particles from an infected individual person’s lips and noise when they sneeze, cough or speak in public place or in a group. The particles size range is between larger respiratory droplets to tiny aerosols. The virus, according to current information, spreads largely among persons who are in close contact to one another, frequently within 1 metre (short-range). Infections occur only when virus containing aerosols or particles are inhaled or come in direct contact with the healthy individual. The virus can also spread in interior spaces that are confined and/or inadequately ventilated, where people prefer to spend extended periods of time. This is as aerosols stays suspended in air or travel a distance of more than 1 to 2 metre (long-range).

 Moreover, the association between temperatures and COVID-19 dispersion in three different eco-geographical regions of India were reported. In contrast to previously reported findings, the rising temperatures did not stop the spread of COVID-19 as widely believed, and there is no link between the temperature regime and rising COVID-19 cases **[**[**12**](file://C:\Users\sanjeev\Downloads\12.Meraj,%20G.,%20Farooq,%20M.,%20Singh,%20S.%20K.,%20Romshoo,%20S.%20A.,%20Sudhanshu,%20Nathawat,%20M.%20S.,%20&%20Kanga,%20S.%20(2020).%20Coronavirus%20pandemic%20versus%20temperature%20in%20the%20context%20of%20Indian%20subcontinent:%20a%20preliminary%20statistical%20analysis.%20Environment,%20Development%20and%20Sustainability.%20doi:10.1007\s10668-020-00854-3)**].**

**OVERVIEW OF INFECTION MECHANISM**

The envelope-anchored spike glycoprotein, which binds to the angiotensin-converting enzyme 2, allows the virus to enter host cells (ACE2). During membrane fusing, the viral RNA sequencing is liberated into the cytoplasmic, and the exposed RNA is processed into two specific proteins and structural proteins. The envelope, genomic RNA, and nucleocapsid proteins are all brand new. Glycoprotein mixes in the endoplasmic reticulum (ER) and the Golgi apparatus to form viral particle buds. The virus is then released after the virion-containing vesicles fuse to the plasma membrane **[**[**13**](file://C:\Users\sanjeev\Downloads\13.Orleans%20L,%20is%20Vice%20H,%20Manchikanti%20L.%20Expanded%20umbilical%20cord%20mesenchymal%20stem%20cells%20(UCMSCs)%20as%20a%20therapeutic%20strategy%20in%20managing%20critically%20ill%20COVID-19%20patients:%20the%20case%20for%20compassionate%20use.%20Pain%20physician.%202020;23:E71-E83.)**].**

Infection with the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) has a significant impact on the immune system. Forming an effective innate immune response followed by a successful adaptive immune response in the early stages of the disease prevents the virus from reaching the alveoli and causing tissue damage.

 The virus causes a mild to severe respiratory infection in this scenario, and the patient heals without needing any specific therapy. If the virus spreads to the lungs, significant inflammatory reactions and cytokine secretions are triggered, followed by widespread cell-mediated immune responses to clear the infected cells. **[**[**13**](file://C:\Users\sanjeev\Downloads\13.Orleans%20L,%20is%20Vice%20H,%20Manchikanti%20L.%20Expanded%20umbilical%20cord%20mesenchymal%20stem%20cells%20(UCMSCs)%20as%20a%20therapeutic%20strategy%20in%20managing%20critically%20ill%20COVID-19%20patients:%20the%20case%20for%20compassionate%20use.%20Pain%20physician.%202020;23:E71-E83.)**].**

The inflammatory response, as well as other long-term implications, is a significant focus of COVID-19 research and more studies are needed to explore. Higher complex cellular organoids or organ-on-a-chip innovations may be more beneficial for studying SARS-CoV-2 disease and stem cell reactions**. [**[**14**](file:///C%3A%5CUsers%5Csanjeev%5CDownloads%5C14.%09Chugh%2C%20R.%20M.%2C%20Bhanja%2C%20P.%2C%20Norris%2C%20A.%2C%20%26%20Saha%2C%20S.%20%282021%29.%20Experimental%20Models%20to%20Study%20COVID-19%20Effect%20in%20Stem%20Cells.%20Cells%2C%2010%281%29%2C%2091.%20doi%3A10.3390%5Ccells10010091)**-15].**

**VACCINE THERAPY:**

Vaccines to prevent the spread of COVID-19 are the best option for putting a stop to the pandemic. However, they are likely to be concerned as long as the US Food and Drug Administration (FDA) continues to allow or authorise the use of COVID-19 immunizations for emergency purposes**. [24]**

**Possible side effects of Covid-19 vaccine:**

A COVID-19 vaccine cause mild side effects after the first or second dose, which including: Fever, Fatigue, Pain, redness or swelling where the shot was given, Headache, Joint pain, Muscle pain, Feeling unwell, Swollen lymph nodes, Nausea and vomiting. (**Table 1)** **[31]**

Several COVID-19 vaccines are currently being studied in clinical trials. The FDA is still evaluating the results of these trials before approving or approving the use of COVID-19 vaccinations. Moreover, because COVID-19 vaccines are in limited supply and vaccine approvals from the FDA can take months or years, the FDA granted immediate use permission for COVID-19 immunizations based on very little information than is usually required. **[25-29]**

 **Table-1: Different Vaccine candidates**

|  |  |  |  |
| --- | --- | --- | --- |
| **S.NO.** | **VACCINES**  | **TYPE** | **COUNTRY OF ORIGIN** |
| 1. | Covaxin (BBV152) | Inactivated vaccine | India |
| 2. | ZyCoV-D | DNA vaccine (plasmid) | India |
| 3. | Moderna COVID‑19 Vaccine (mRNA-1273); also called Spikevax | mRNA-based vaccine | US |
| 4. | COVID-19 Vaccine Janssen (JNJ-78436735; Ad26.COV2.S) | Non-replicating viral vector | Netherlands, US |
| 5 | AstraZeneca (AZD1222)Covidshield | Adenovirus vaccine | UK |
| 6. | Sputnik V | Recombinant adenovirus vaccine (rAd26 and rAd5) | Russia |
| 7. | EpiVacCorona | Peptide vaccine | Russia |
| 8. | CoviVac | Inactivated vaccine | Russia |
| 9. | CoronaVac | Inactivated vaccine (formalin with alum adjuvant) | China |
| 10. | BBIBP-CorV | Inactivated vaccine | China |
| 11. | Convidicea (PakVac, Ad5-nCoV) | Recombinant vaccine (adenovirus type 5 vector) | China |
| 12. | WIBP-CorV | Inactivated vaccine | China |
| 13. | ZF2001 (ZIFIVAX) | Recombinant vaccine | China, Uzbekistan |
| 14. | QazVac (QazCovid-in) | Inactivated vaccine | Kazakhstan |
| 15. | COVIran Barekat | Inactivated vaccine | Iran |
| 16. | Soberana 02/Soberana Plus | Conjugate vaccine | Cuba, Iran |

**COVIDSHIELD**

**Manufacturer:** University of Oxford Research, AstraZeneca.

**Name:** AZD1222

**Type pf vaccine:** Non-Replicating Viral Vector

**Administration method:** Intramuscular injection (IM)

**Mechanism of Immunization:** This vaccination only produces antibodies against a part of the virus. A strand of DNA that encodes for the spike protein has been included (S-protein). Once inside the cells, the DNA component must first reach the nucleus to generate its mirror image (complementary RNA). The RNA then goes to the cytoplasm as a messenger, where it initiates the creation of S-protein throughout a ribosome. S-protein-induced immunity could not have been as available in natural resistance as Covaxin-induced immunity. **[17]** It's uncertain if the DNA material that persists inside the nucleus has any long-term effects (for example, incorporation into human DNA).

**COVAXIN**

**Manufacturer/developer:** Bharat Biotech ICMR

**Name:** (BBV 152)

**Vaccine type:** Inactivated vaccine

**Method of immunization:** Antibodies can be produced against multiple distinct sections of the virus using this vaccination. The immunity generated by this vaccine will be more widespread and similar to that elicited by infection since it comprises a completely inactivated virus with all 29 proteins intact. This excludes any genetic material with the ability to replicate or reach the nucleus, although it does provide immunity against pathogenic proteins other than the S-protein. This is built on a technological platform that has already been utilised in other vaccines, including the polio vaccine. These immunizations, however, require an adjuvant to promote immunity. Alum is frequently employed for this purpose, however it mostly stimulates Th-2 immunity, which has more unfavourable consequences. As a consequence, Bharat Biotech has used "Algel-IMDG (Imidazoquinolinone)," a different adjuvant that stimulates Th-1 type immunity, which is also induced by mRNA/DNA vaccines. **[16-19]**

**SPUTNIK V**

**Manufacturer/developer:** Gamaleya Research Institute of Epidemiology and Microbiology, Russia.

**Vaccine type:** Recombinant adenovirus vaccine (rAd26 and rAd5)

**Mechanism of Immunization:** Sputnik V uses a virus that has been attenuated to deliver small amounts of a pathogen and elicit an immune response. The Sputnik V (Gam-COVID-Vac) vaccine accelerates the development of protection against SARS-CoV-2, the beta corona virus that caused the COVID-19 pandemic. **[29]**

**MODERNA**

**Manufacturer/developer:** ModernaTX, Inc.

**Name:** mRNA-1273

**Vaccine type:** mRNA-based vaccine

**Mechanism of Immunization:** The AstraZeneca vaccine employs a modified chimpanzee DNA adenovirus that has never been exposed to humans and only elicits an immune response to the viral protein encoded in the host DNA, not the adenovirus itself. The DNA vector encodes a protein that is identical to the viral s-peptide in order to elicit an immune response against the virus. The DNA vector is used as a template in human cells to make new chimp adenovirus replicas and produce the viral protein that causes an immune response. The chimp adenovirus is injected into humans and latches on to the host cells. DNA is released into the cytoplasm before migrating to the cell's nucleus. **[18]**

It is not integrated into cellular DNA, but rather converted to mRNA by host enzymes, which migrates back into the cytoplasm and links with free or tethered endoplasmic reticulum ribosomes to create translated proteins. When MHC1 and MHC2 proteins are expressed on cell membranes, they form complexes. The activation of T-, B-, and plasma cells, as well as antibodies, is the same for both RNA and DNA vaccines at this point**.[25]**

**JANSSEN (JOHNSON & JOHNSON)**

**Manufacturer/developer:** Janssen Pharmaceuticals Companies of Johnson & Johnson

**Vaccine type:** Non replicating viral vector

**Mechanism of Immunization:** This vaccine uses a virus that isn't harmful to humans (adenovirus 26 CoV2) to deliver a gene that has the blueprint for the coronavirus's spiky protein. The vaccine's mode of action is similar to that of AstraZeneca's vaccine. In the lab, genetic information for the spike-protein in the viral DNA that may synthesise a particular mRNA is added to an adenovirus vector**. [28]**

 The adenovirus's DNA parts that allow it to multiply were removed from the vector, and as a result, the vector cannot replicate in human cells. The vector clamps on to human cells, and the DNA holding the SARS-CoV-2 spike protein information is transported into the nucleus without being integrated into the host cell DNA.

The strand of viral DNA that would usually instruct the cell to generate more adenovirus particles is translated into mRNA and delivered to the cytoplasm, where the cell machinery produces spike protein rather than adenovirus particles. T-cells (CD4 and CD8), B-cells, interleukin (IL), and plasma cells generate the several primary immune responses (killer CD8 T-cells, antibodies, and helper CD4 T-cells) to halt the infection, which are triggered by viral spike proteins on the cell surface. When infectious virus particles are present circulate outside of cells, antibodies are efficient in protecting uninfected cells, but helper T-cells are required for the death of previously infected human cells (antibodies can easily bind onto spike proteins on the viral surface) **[29-35]**

**CONCLUSION**

The only way to be protected from COVID-19 spread is by getting vaccinated. The vaccine development efforts have been seriously a good attempt towards this pandemic and our vaccination program moved swiftly, and many vaccines have been approved and several major are moving towards clinical trials for evaluation. These include traditional recombinant proteins, replicating, and nonreplicating viral proteins, and mRNA approaches. Several vaccinations have been developed or are being developed across the world. The vaccine candidates which make use of a novel technique based on mRNA molecules for spike protein synthesis that are incorporated in a lipoid particle that does not interact with other mRNAs. These mRNA vaccines are less complicated than protein vaccines, which are more complex to create and need more time for FDA clearance due to the several stages that must be reviewed. The production process for every specific protein is complicated, but the procedure for RNAs is consistent. Within 10 months, the successful Pfizer and Moderna vaccines received licensure.

 Each of these vaccines have one thing in common that we should be given 2 shots of the vaccine through (IM) route but different dosage and different time to administer according to their efficiency and mode of action. Several companies are developing nucleic acid –based vaccines, including Moderna, BioNTech / Pfizer, CureVac (mRNA-based) etc.

It's encouraging to see how quickly vaccine development efforts have progressed, and that several major vaccine platforms are nearing clinical trials. Conventional recombinant protein methodologies, replicating and nonreplicating viral vectors, and nucleic acid mRNA and DNA approaches are among them. Each of these vaccine platforms has benefits and drawbacks. Important characteristics include manufacturing speed and flexibility, safety and reactogenicity, the profile of humoral and cellular immunogenicity, immunity durability, manufacturing scale and cost, vaccine stability, and cold chain requirements.

Countries have approved different vaccines according to which they are getting every individual vaccinated as the main vector for the spread of these deadly virus is human being itself. In future, we may find a permanent solution to it as our scientist are working on it but till then we have to rely on the vaccines only.

The next-generation Covid-19 vaccines have improved immunisation regimens that will allow people to return to their regular lives. Next-generation vaccinations will be able to guard against viruses with spike mutations by eliciting larger and more robust T-cell responses than current immunizations. Another protein to consider is the viral structural nucleocapsid (N), which may boost the cellular immune response.

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