



## CORONAVIRUSES AND POTENTIAL VACCINES

## Medical Microbiology

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## ABSTRACT

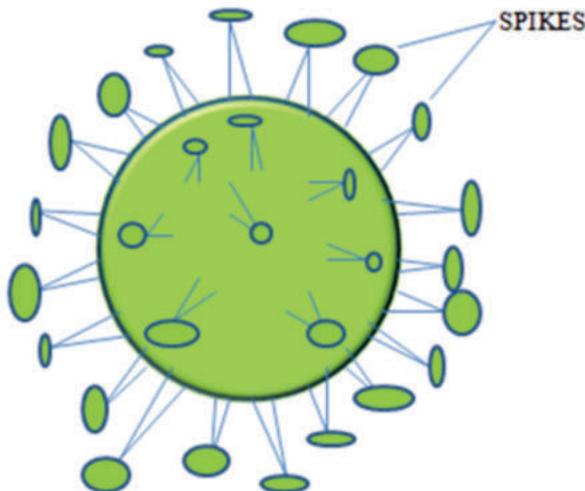
It is believed that CoVs might have been transmitted to humans via animals. Those causing SARS, MERS and COVID-19 probably have originated from bats. Possibly the transfer of the new CoV strain from the original host species to humans must have involved another animal species which acted as an intermediate host. The SARS-CoV-2, is most closely related to a group of SARS-CoVs found in humans, bats, pangolins and civets. As the virus was new, it potentially infected very large numbers of people all around the globe and thus resulted into pandemic. Even though the number of very severe cases was low in terms of percentage but taking it into terms of number it becomes a very large count of people with acute illness. SARS-CoV-2 infected patients reportedly develop low titre neutralizing antibody and usually suffered prolonged illness, that showed a more effective SARS-CoV-2 immune surveillance evasion when compared with SARS-CoV. Various treatments were tried and different vaccines were tested out to fight against this deadly virus all around the globe. In this article, a brief review of information on different CoVs and its various vaccine has been made.

## KEYWORDS

SARS(Severe Acute Respiratory Syndrome), MERS(Middle East Respiratory Syndrome), SARS-CoV-2(Severe Acute Respiratory Coronavirus-2), CoV(Coronavirus), R0(Reproduction Number).

## INTRODUCTION

CoVs are single-standard (ss) positive RNA viruses which are characterized by club-like spikes of protein (glycoprotein) which are present on the surface of viruses and these spikes gives virions a crown-like appearance, the role of these spikes is to help the virus by binding to and infecting healthy cells. Moreover, these spikes also allows the immune system to detect the virus in the host cell. Bits of these spikes are used in potential CoV vaccines that help the body to produce antibodies against these new viruses.



**Figure 1: Diagrammatic representation of CoV with Spikes.**

- SARS (2002-2003): In SARS outbreak (China), most of the new patient cases had animal exposure before developing the disease. Investigations confirmed that SARS-CoV strains were transmitted to palm civets from other animals [1, 2]. Later, it was reported that discovery of coronaviruses related to human SARS-CoV, which were named SARS-like coronaviruses or SARS-CoVs, in horseshoe bats [3, 4]. According to these, bats may be the natural reservoirs for the virus and that palm civets are only intermediate hosts [5, 6]. The various symptoms of a SARS-CoV infection are; fever, fatigue, muscle pain, headache, loss of appetite, diarrhoea, shivering, dry cough, breathing difficulties and low levels of oxygen in blood.

SARS-CoV is an airborne virus that spreads through small droplets of saliva released into the air through coughs and sneezes which infects another person when they breathe in these droplets and also via fomites such as door handles and faeces when proper hygiene is not maintained. At the beginning of the outbreak in 2002, the R0 value was estimated between 2.0 and 3.0. In absence of intervention and

control measures the R0 of SARS was about 3. As there is no vaccine for SARS-CoV thus any suitable treatment can be supportive. This means the body is supported while it fights the virus naturally, with ventilators to assist breathing, antibiotics to kill bacteria that cause pneumonia or steroids for reducing inflammation in lungs.

- MERS (2012): Most of the MERS cases had previous contact with dromedary camels. The MERS-CoV strains isolated from camels were almost identical to those isolated from humans [7, 8], and the MERS-CoV isolates were found highly prevalent in camels from the Middle East, Africa, and Asia [9, 10]. Generally, all of the related MERS-CoVs isolated from bats support the hypothesis that MERS-CoV originated from bats [11]. This is a zoonotic virus which is transmitted between animals and people. Humans are infected through direct or indirect contact with infected dromedary camels after which human-to-human transmission is possible. The R0 of MERS in secondary cases was about 0.69 [12]. Whereas, range of R0 values without control was estimated around 0.8-1.3 [13].

The infection in MERS-CoV ranges from asymptomatic or mild to severe respiratory symptoms and death. Typical symptoms are; fever, cough, shortness of breath, gastrointestinal symptoms including, diarrhoea and pneumonia. The treatment for MERS patients was largely based on the experience of treating SARS. Considering convalescent plasma, interferons, lopinavir and mono- or polyclonal antibodies for the treatment.

- SARS-CoV-2 (2019): The 1st case was reported in Wuhan, China; this virus is characterized by a unique combination of polybasic cleavage sites, a distinctive feature known to increase pathogenicity and transmissibility in other viruses [14]. Even though bats are likely to be the reservoir host; their general biological differences from humans make it feasible that some other mammalian species acted as an intermediate host, in which SARS-CoV-2 obtained some or all of the mutations necessary for effective human transmission. One of the suspected intermediate hosts is Malayan pangolin. This virus causes mild symptoms in most cases and many people are asymptomatic. Possible symptoms of infection are; high temperature, continuous dry cough, loss of taste and smell.

The transmission of virus occurs mainly through mucus droplets released by an infected person through coughing, sneezing, or talking directly attack the healthy person or through secondary sources like any object contaminated with virus. The approximate R0 value is 2.5 and the treatment for SARS-CoV-2 is also supportive. The body is supported while it fights the virus naturally with ventilators that assist breathing and maintain good oxygen levels in blood. Many drugs have been tested out as therapeutic measures and different ones are being used around the world.

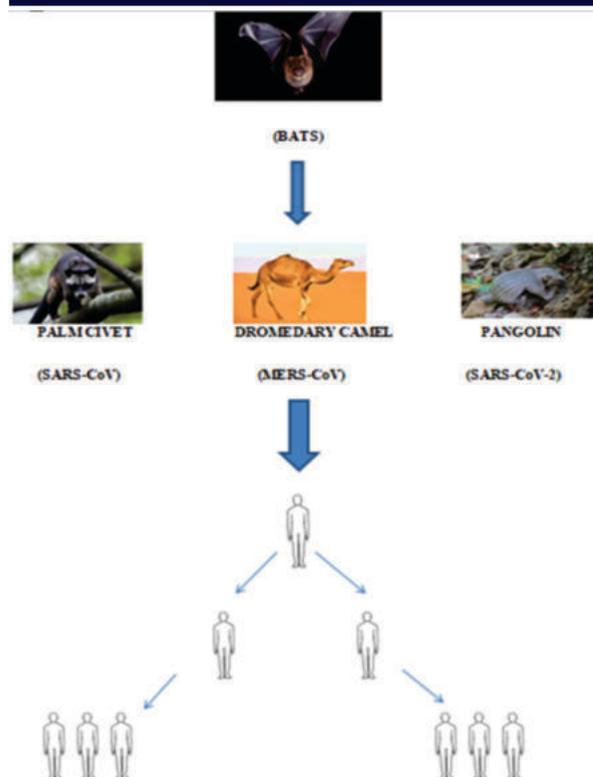


Figure 2: Flowchart depicting transmission of CoVs.

#### VACCINES:

**1. PFIZER:** Pfizer- BioNTech vaccine (Comirnaty) was approved by Food and Drug Administration (FDA) in August 2021. Prior to its approval, it was the first COVID-19 vaccine to admit FDA Emergency Use Authorization (EUA) back in December 2020, after this it was reported by company that its vaccine was largely effective at precluding characteristic complaint. This is a type of messenger RNA (mRNA) vaccine.

**INGREDIENTS:** It contains Nucleoside-modified mRNA that encodes the viral spike (S) glycoprotein of SARS-CoV-2, 2[(polyethylene glycol (PEG))-2000]-N,N-ditetradecylacetamide, ((4-hydroxybutyl) azanediyl) bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 1,2-distearoyl-sn-glycero-3-phosphocholine, Sucrose, plant derived cholesterol, Tromethamine, Tromethamine hydrochloride [15].

Here, the mRNA provides instructions to the body to build a harmless piece of protein from the virus that causes COVID-19. This protein causes an immune response that helps protect the body from COVID-19 in the future and the lipids content helps the mRNA to enter cells; whereas, sugar and acid stabilizers work together to keep vaccine molecules stable while the vaccine gets manufactured, frozen, shipped and stored until it is ready for vaccine recipient.

**MECHANISM OF ACTION:** Comirnaty has nucleoside modified mRNA (modRNA) encapsulated in lipid nanoparticles that delivers the modRNA into host cells. The lipid nanoparticle formulation facilitates the delivery of RNA into human cells. Once inside these cells, the modRNA gets translated by host machinery to produce modified SARS-CoV-2 spike (S) protein antigen, which gets subsequently recognized by the host immune system. Comirnaty has been shown to elicit both neutralizing antibody and cellular immune responses to the S protein, which helps protect against subsequent SARS-CoV-2 infection [16].

**POSSIBLE SIDE EFFECTS:** Pain, redness, or swelling at the site of shot administered, and/or tiredness, muscle pain, fever, chills, headache, or nausea throughout the body. Few side effects are serious, but rare like anaphylaxis, a severe reaction but is treatable with epinephrine [17, 18].

**2. COVISHIELD:** The Covishield vaccine was developed by Serum Institute of India Pvt. Ltd. It's a weakened version of a common cold virus (adenovirus); recommended by WHO on February 2021.

**INGREDIENTS:** This vaccine is made of ChAdOx1 nCoV-19 CoV

Vaccine (Recombinant), the single dose of vaccine contains  $5 \times 10$  virus particles ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant)

Here, recombinant is replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 spike glycoprotein and is produced in genetically modified human embryonic kidney (HEK) 293 cells. The Covishield vaccine includes the following ingredients: L-Histidine, L-Histidine hydrochloride monohydrate, Disodium edetate dihydrate (EDTA) Polysorbate 80, Sucrose, Ethanol, Magnesium chloride hexahydrate, Sodium chloride, Water for injection.

**MECHANISM OF ACTION:** COVISHIELD is a monovalent vaccine that is composed of single recombinant, replication-deficient chimpanzee adenovirus (ChAdOx1) vector encoding the S glycoprotein of SARS-CoV-2. Following administration, the S glycoprotein of SARS-CoV-2 is expressed locally stimulating cellular immune responses and neutralizing antibody.

**POSSIBLE SIDE EFFECTS:** This vaccine can cause side effects just like any other medicine, although not everybody gets them. Such reactions may include following symptoms: feeling faint or light-headed, shortness of breath or wheezing, changes in heartbeat, fever, swelling of your lips, face, or throat and headache [19].

**3. JANSSEN:** It is viral vector vaccine which uses a harmless, modified version of a different virus (a vector virus) and not the virus that causes COVID-19. This Johnson & Johnson's coronavirus vaccine under brand name: Janssen was authorized by FDA in February 2021. But the concerns over rare blood clots associated with the vaccine prompted the government to put a pause on it in the spring 2021, which was soon lifted. New restrictions in May were put by FDA on who can get the J&J vaccine based on another review of data on the life-threatening clots.

**INGREDIENTS:** The J&J/Janssen COVID-19 vaccine contains only the following ingredients; Recombinant, replication-incompetent Ad26 vector, encoding a stabilized variant of the SARS-CoV-2 Spike (S) protein, 2-hydroxypropyl- $\beta$ -cyclodextrin, Polysorbate-80, Sodium chloride, Trisodium citrate dehydrate, Citric acid monohydrate, Ethanol.

A version of harmless virus that is unrelated to the COVID-19 virus provides instructions to the body which are used to build a harmless piece of a protein from the virus that causes SARS-CoV-2. This protein causes an immune response that helps protect the body from COVID-19 in the future whereas, sugars, salts, acid and acid stabilizer work together to keep the vaccine molecules stable while its manufacturing, shipping, storing is done.

**MECHANISM OF ACTION:** This is a carrier vaccine, which uses a different approach than the mRNA vaccines to instruct human cells to make the SARS-CoV-2 spike protein. A harmless adenovirus carries genetic code on the spike proteins to the cells. The shell and the code can't make us sick but once the code gets inside the cells, the cells produce spike protein to train the body's immune system that generates antibodies and memory cells to protect against actual SARS-CoV-2 infection.

**POSSIBLE SIDE EFFECTS:** Pain, redness, swelling where the shot was administered; tiredness, nausea, muscle pain, headache, chills, fever throughout the body [15].

**4. SINOPHARMA:** Sinopharm's BBIP-CorV may be a form of inactivated vaccine prepared from particles of virus that lacks disease producing capability. China National Pharmaceutical Group Co. Ltd. Together with Beijing Institute of Biological Products Co. developed this vaccine in 2020.

**INGREDIENTS:** The liquid formulation contains  $4 \mu\text{g}$  total proteins with aluminum hydroxide adjuvant (0-45mg/ml) per 0.5 ml.

**MECHANISM OF ACTION:** BBIP-CorV is formed using inactivated CoVs in which the inactivated viruses are mixed with very little amount of aluminium-based compound called "adjuvant", this stimulates the system. This helps in production of antibodies against SARS-CoV-2 and then antibodies get attached to the viral spike proteins thus preventing the entry of viruses within the cell.

**POSSIBLE SIDE EFFECTS:** The common possible side effects are often injection site reactions, headaches, fatigue, nausea, encephalomyelitis. There was also one diagnosis of thrombus (blood clot) within the vaccine group. [20].

#### CONCLUSION

As all the CoVs typically have common origin and are somewhat genetically similar but have potential to cause infections at different levels as a result of mutation in them. These resulted in mild to severe infections which became epidemic and pandemic that caused numerous lives around the globe. No particular treatment has been assigned for these CoVs but for SARS-CoV-2 many vaccines were developed in short period of time which have different content and mode of action; trying to stop the dreadful virus and serve humanity.

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