# Medicines and Vaccines in Dealing with Covid-19

Xianyi Zheng[a]
*Li Po Chun United World College of Hong Kong, HKSAR, China*

Keywords: SARS-CoV-2, Covid-19, Medecines, Vaccines.

Abstract: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)(Wikipedia 2021) has several components, including spike protein and membrane protein, and has several variants. Currently, remdesivir and dexamethasone are two common medicines that are used for treatments of the Covid-19 disease. It has been shown that the recovery time for patients who were treated with these two drugs was much shorter than patients who did not treat with them and the mortality of patients who were treated with them was lower than patients who did not. Also, several vaccines, including vaccines produced by Moderna, vaccines produced by BioNTech/ Pfizer, and vaccines produced by Oxford/ AstraZeneca have shown efficacies in preventing infection of the virus. The efficacies of these three vaccines towards original SARS-CoV-2 were all above 70%, for which vaccine produced by Moderna, vaccine produced by BioNTech/ Pfizer was around 94.5% (Moderna, Inc. 2020) and 95%)(Polack et al. 2020), and that of Oxford/ AstraZeneca was around 70%(NEEDHAM 2020). However, when dealing with SARS-CoV-2 variants, the efficacies of these three vaccines decreased. In conclusion, although different medicines and vaccines have been used to prevent the exacerbation of the Covid-19 pandemic, the emerge of SARS-CoV-2 variants is still a challenge as these variants decrease the efficacies of vaccines and increase the infection rate.



## 1 INTRODUCTION

A new type of coronavirus (severe acute respiratory syndrome coronavirus 2) was rapidly spread in Wuhan, China, in late 2019. Although many governments and non-government organizations put a large number of financial resources into tackling the pandemic, it is hard to observe the turning point of this pandemic until now, and the future course of this virus is still unknown. Many companies and institutions have been trying to invent vaccines and medicines based on the structure of COVID-19, and some of them have major breakthroughs on vaccines and medicines. This paper would illustrate the basic structure of coronavirus and give a broad overview of the current medicines and the development of vaccines. Topics discussed in the paper give the newest update to understand the current situation of the pandemic, which is essential to the fundamental development of different research.

## 2 STRUCTURE OF SARS-COV-2

SARS-CoV-2 is a single-stranded RNA-enveloped virus (figure 1), and like other viruses, it cannot survive without a host cell. This virus has been reported that it has more than 95% homology with the coronavirus in the bat's body and more than 70% similar to the SARS-CoV. RNA of the virus gives its structure and enables it to replicate. It has structural proteins, such as the S (Spike) protein, the E (Envelope) protein, the M (Membrane), and N (Nucleocapsid) proteins, and non-structural proteins, such as 3-chymotrypsin-like protease, papain-like protease, and RNA-dependent RNA polymerase(Huang, Yang, Xu, Xu, and Liu 2020).

### 2.1 Spike Protein

The spike protein gives the virus a "corona" structure. For spike protein (figure 1), it is responsible for a virus to attach to the membrane of the host cell, and it has two functional subunits (figure 2), which are S1 and S2. The S1 subunit consists of the N-terminal

[a] https://orcid.org/0000-0003-1467-1342



Zheng, X.
Medicines and Vaccines in Dealing with Covid-19.
DOI: 10.5220/0011248000003443
In *Proceedings of the 4th International Conference on Biomedical Engineering and Bioinformatics (ICBEB 2022)*, pages 601-611
ISBN: 978-989-758-595-1

domain (NTD) and receptor-binding domain (RBD) (Huang, Yang, Xu, Xu, Liu 2020), which allows it to bind to the host cell receptor. The S2 subunit comprises of fusion peptide (FP), heptad repeat 1 (HR1), central helix (CH), connector domain (CD), heptad repeat 2 (HR2), transmembrane domain (TM), and cytoplasmic tail (CT) (Huang, Yang, Xu, Xu, and Liu 2020) (Figure 3), which allows it to mediate the fusion of viral and cellular membranes. The receptor-binding domain (RBD) recognizes a specific receptor called the ACE2 (angiotensin-converting enzyme receptor 2). It has shown that the binding of ACE2 receptor with RBD is at least the same affinity and potentially as much as 20 times greater affinity than the SARS virus. Such high infinity could be one of the explanations for the reasons why it spreads so easily.

## 2.2 Membrane Protein

The membrane protein (figure 1) is the most abundant protein on the viral surface and defines the shape of the viral envelope. It likes a central organizer for coronavirus assembly and interacts with the other structural proteins on the viral membrane.

## 2.3 Other Components and Nucleocapsid Protein

The viral envelope (figure 1), a fatty layer, is underneath the surface proteins derived from the host cell membrane. When it contacts with soap, it will break down and die, which suggests that handwashing with soap is essential to prevent the spread of this virus.

Underneath this layer is a capsid, a protein shell that encloses the virus's genetic material. Inside this capsid, nucleocapsid proteins (figure 1) can be found. These proteins are bound to the virus's single strand of RNA, which is the place where genetic information is held to allow the virus to replicate. Nucleocapsid protein is multifunctional. It essentially inhibits a lot of host cells defense mechanisms and assists the viral RNA in replicating itself and, therefore, in creating new viral particles.

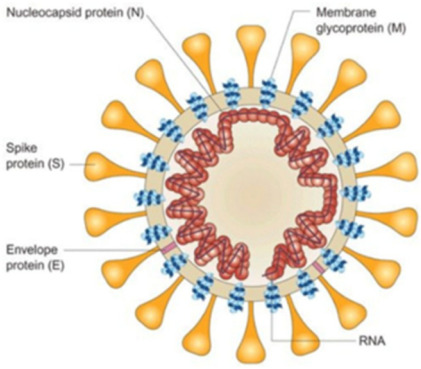


Figure 1: (LubioScience 2020). Structure of SARS-CoV-2.

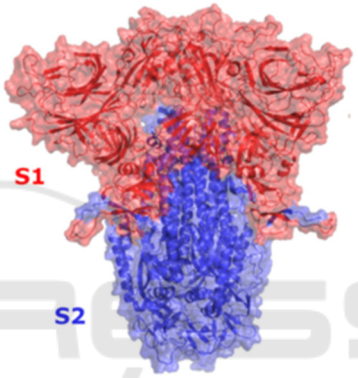


Figure 2: (Mansbach, Chakraborty, Nguyen, Montefiori, Korber, Gnanakaran 2021). Structure of spike protein.

# 3 SYMPTONS OF DISEASE

## 3.1 Transmission of COVID-19 Infection

People of all ages can be infected by this virus. Infection is transmitted through a droplet of saliva or snivel generated during talking, coughing, or sneezing of symptomatic patients but can also occur from asymptomatic people. Also, contact surface spread, which means that directly touching the surface which has viruses on it, is possible for virus transmission, and it has been reported that this type of virus can be transmitted through the air.

## 3.2 Symptoms

Typically, COVID-19 symptoms begin one to fourteen days after exposure to the virus. On average, it takes 5–6 days from when someone is infected with the virus for symptoms to

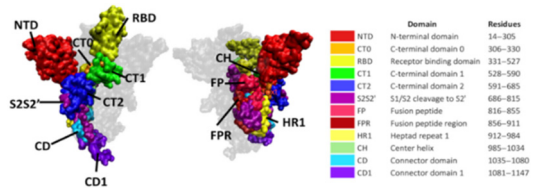


Figure 3: (Mansbach, Chakraborty, Nguyen, Montefiori, Korber, Gnanakaran 2021): Detail structure of spike protein.

show; however, it can take up to 14 days. Around one in five infected individuals do not develop any symptoms. Most people have mild symptoms, and the most common mild symptoms of COVID-19 are fever, dry cough, and fatigue(Wikipedia 2021). Also, other mild symptoms that are less common but still can affect some people, including loss of taste or smell, nasal congestion, conjunctivitis (also known as red eyes), sore throat, headache, muscle or joint pain, different types of skin rash, nausea or vomiting, diarrhea, and chills or dizziness(World Health Organization 2021). However, some may have severe symptoms, including shortness of breath, loss of appetite, confusion, persistent pain or pressure in the chest, high temperature(above 38 °C) (World Health Organization 2021). Other less common severe symptoms include irritability, confusion, reduced consciousness (sometimes associated with seizures), anxiety, depression, sleep disorders, and more severe and rare neurological complications such as strokes, brain inflammation, delirium, and nerve damage (Wikipedia 2021). Some people even develop acute respiratory distress syndrome (ARDS). ARDS can be precipitated by cytokine storms, multi-organ failure, septic shock, and blood clots (Wikipedia 2021). Longer-term damage to organs (in particular, the lungs and heart) has been observed (Wikipedia 2021).

# 4 VARIANTS OF SARS-COV-2

Variants of SARS-CoV-2 are caused by the mutation of the genetic sequence of the virus. The mutation of the genetic sequence of a virus can affect its property, such as transmissibility. Up to August 2021, there are many variants of SARS-CoV-2, and four of them: Alpha, Beta, Gamma, and Delta, are listed in currently designated variants of concern according to the World Health Organisation(World Health Organization 2021). Apart from these four variants, lambda variant, another variant of SARS-CoV-2, is also under concern.

## 4.1 Alpha

The Alpha variant, also known as lineage B.1.1.7, was first documented in the United Kingdom in September 2020(World Health Organization 2021). It has been found that the transmissibility of this variant is around 29%, substantially higher than the original one. One of the most important differences between the original virus and the Alpha one is the amino acid in position 501. In the Alpha variant, the amino acid position 501 is tyrosine instead of asparagine. Such changes in amino acids cause changes in the receptor-binding domain (RBD), which changes the specificity of the binding between human ACE2 receptors and RBD(Wikipedia 2021). This allows viruses to become more infectious.

## 4.2 Beta

The beta variant, also known as lineage B.1.351, was first recorded in South Africa in May 2020 (World Health Organization 2021). It has also been proved that the transmission rate of this variant is higher than the original one. There is a total of eight mutations in the spike proteins in this virus, including K417N (a change from lysine to asparagine in amino acid position 417), E484K (a change from glutamic acid to lysine in amino acid position 484), and N501Y (a change from asparagine to tyrosine in amino acid position 501) (Wikipedia 2021). Similar to the situation in the alpha variant, these mutations cause changes in the receptor-binding motif (RBM) of the receptor-binding domain (RBD), which allows the beta variants to spread faster.

## 4.3 Gamma

The gamma variant, known as lineage P.1, is one of the variants of SRAS-CoV-2. It was first recorded in Brazil in November 2020(World Health Organization 2021). This variant has ten amino acids mutations, including N501Y (a change from asparagine to tyrosine in amino acid position 501), E484K (a change from glutamic acid to lysine in amino acid position 484), and K417T (a change from lysine to threonine in amino acid position 417) (Wikipedia 2021). It has been shown that the transmission rate is

approximately 38%, which is higher than that of the alpha variant.

### 4.4 Delta

The delta variant, known as lineage B.1.617.2, has the highest transmissibility of all discovered variants. It was first identified in India in October 2020 according to the WHO(World Health Organization 2021). Mutations, D614G (an aspartic acid-to-glycine substitution at amino acid position 614), T478K (a threonine-to-lysine substitution at amino acid position 478), L452R (a leucine-to-arginine substitution at amino acid position 452), and P681R (a proline-to-arginine substitution at amino acid position 681), are found in delta variants (Wikipedia 2021). The common symptoms of the delta variant have changed. Headaches, sore throat, a runny nose, and fever are common symptoms of this variant(healthline 2021).

### 4.5 "Delta Plus"

"Delta plus" variant is a delta variant with K417N mutation (a lysine-to-asparagine substitution at amino acid position 417) (Wikipedia 2021).

### 4.6 Lambda

Lambda variant, known as lineage C.37, was first detected in Peru in December 2020. G75V, T76I, L452Q, F490S, D614G, and T859N mutations and a 7-amino-acid deletion in the NTD (RSYLTPGD246-253N) were found in the spike protein of the lambda variant(Kimura et al. 2021). It has been shown that this variant is more infectious, and the deletion in NTD is responsible for neutralizing antibiotics (Kimura et al. 2021).

## 5 CURRENT MEDICINES

Two common medicines – remdesivir and dexamethasone -- that are used for the covid-19 treatment would be discussed below.

### 5.1 Remdesivir

Remdesivir is one of the most common medicines that is used for the treatment of COVID-19 because it has been shown in research that it is efficacious. Remdesivir is an intravenous nucleotide prodrug of an adenosine analog. Remdesivir binds to the viral RNA-dependent RNA polymerase, inhibiting viral replication through premature termination of RNA transcription(NIH 2021).

#### 5.1.1 Analysis of the Research of Remdesivir

In the research, there were 1114 patients who were assessed for eligibility: 1062 of them underwent randomization; 541 of them were allocated to the remdesivir group, and 521 were placed to the placebo group(Beigel et al. 2020). The primary analysis was a stratified log-rank test of the time to recovery with remdesivir as compared with placebo, with stratification by disease severity(Beigel et al. 2020).

#### 5.1.2 Primary Outcome

Patients in the remdesivir group (median: 10 days; rate ratio of recovery: 1.29) recovered faster than patients in the placebo group (median: 15 days) (Beigel et al. 2020). The 95% confidence interval (CI) and the probability of extreme cases were 1.12-1.49 and <0.001 (Beigel et al. 2020). Among patients who were hospitalized and required any supplementary oxygen, the rate ratio for recovery was 1.45 (95% CI, 1.18 to 1.79) (Beigel et al. 2020); among patients who were hospitalized and did not require any supplementary oxygen but required ongoing medical care and those who were hospitalized and required noninvasive ventilation or use of high-flow oxygen devices, the rate ratio of recovery were 1.29 (95% CI, 0.91 to 1.83) and 1.09 (95% CI, 0.76 to 1.57), respectively(Beigel et al. 2020). The rate ratio for recovery was 0.98 (95% CI, 0.70 to 1.36) for those receiving mechanical ventilation or ECMO at enrollment(Beigel et al. 2020). Patients who underwent randomization during the first 10 days after the onset of symptoms had a rate ratio for recovery of 1.37 (95% CI, 1.14 to 1.64), which was higher than that of those who underwent randomization more than ten days after the onset of symptoms (1.20; 95% CI, 0.94 to 1.52) (Beigel et al. 2020). P value in this experiment is very small, which means that the probability of extreme cases in this research is very small. Also, high confidence interval (CI), 95% (Beigel et al. 2020), ensures the accuracy of the primary outcome in the research of remdesivir.

#### 5.1.3 Key Secondary Outcome

Mortality of patients in the remdesivir group was numerically lowered than those in the placebo group, but the difference was not significant (hazard ratio, 0.55; 95% CI, 0.36 to 0.83) (Beigel et al. 2020). The mortality by 14 days was 6.7% and 11.9% in the remdesivir and placebo groups, respectively(Beigel et

al. 2020). The mortality rate by day 29 was estimated to be 11.4% in remdesivir group and 15.2 in placebo group, respectively (hazard ratio, 0.73; 95% CI, 0.52 to 1.03) (Beigel et al. 2020). Patients in the remdesivir group (24.6%) who had serious adverse events were lower than those in the placebo group (31.6%); patients in the remdesivir group who suffered from serious respiratory failure (8.8%) were lower than those in the placebo group (15.5%)(Beigel et al. 2020). However, patients in the remdesivir group who suffered from pyrexia were higher than those in the placebo group. Other comparisons of safety outcomes are shown in Table 1. Therefore, it can be observed that the possibility of serious adverse events occurred in the remdesivir group is much less than that in the placebo group.

## 5.2 Dexamethasone

Dexamethasone is a corticosteroid that has been recommended by the National Health Service in the UK and the National Institutes of Health (NIH) in the US for the treatment of the Covid-19. It is used to treat those who are very ill, and it has been shown that patients who were treated with dexamethasone recovered faster because dexamethasone can modulate inflammation-mediated lung injury caused by the SRAS-CoV-2 and thereby reduce progression to respiratory failure and death(Engl 2021).

Table 1: A Table showing the negative effects of remdesivir. All the data is collected from Remdesivir for the Treatment of Covid-19 — Final Report (Beigel et al. 2020).

| Events | Remdesivir group | Placebo group |
|---|---|---|
| Total serious adverse event occurred | 131 out of 531 patients (24.6%) | 163 out of 516 patients (31.6%) |
| Serious respiratory failure adverse events | 47 patients (8.8%) | 80 patients (15.5%) |
| Acute respiratory failure, hypotension, viral pneumonia, and acute kidney injury | Less common | More common |
| Death related to treatment assignment | No | No |
| Anemia or decreased hemoglobin | 43 events (7.9%) | 47 events (9.0%) |
| Acute kidney injury, decreased estimated glomerular filtration rate or creatinine clearance, or increased blood creatinine | 40 events (7.4%) | 38 events (7.3%) |
| Pyrexia | 27 events (5.0%) | 17 events (3.3%) |
| Hyperglycemia or increased blood glucose level | 22 events (4.1%) | 17 events (3.3%) |
| Increased aminotransferase levels including alanine aminotransferase, aspartate aminotransferase, or both | 22 events (4.1%) | 31 vents (5.9%) |

### 5.2.1 Samples of the Research of Dexamethasone

In this research, a total of 6425 patients underwent randomization, where 2104 of them were assigned to receive dexamethasone, and 4321 of them received usual care(Engl 2021). The mean age of the patients in this research was 66.1±15.7 years(Engl 2021). 36% of them were female, and 18% were Black, Asian, or from a minority ethnic group(Engl 2021).

### 5.2.2 Primary Outcome and Secondary Outcome

At 28 days, mortality of those who received treatment of dexamethasone (22.9%) was lower than that of those who received usual treatments (25.7%) (rate ratio, 0.83; 95% confidence interval [CI], 0.75 to 0.93; P<0.001) (Engl 2021). Among patients receiving invasive mechanical ventilation, the incidence of death in the dexamethasone group (29.3%) was lower than that in the usual care group (41.4%) (rate ratio, 0.64; 95% CI, 0.51 to 0.81) (Engl 2021). However, no obvious effect of dexamethasone could be seen among patients who were not receiving any respiratory support at randomization(Engl 2021).

### 5.2.3 Secondary Outcome and Other Prespecribe Clinical Outcomes

Patients who received dexamethasone as treatment (median: 12 days) had a shorter duration of hospitalization than those who received usual care (median: 13days) and had a greater probability of discharging alive(Engl 2021). The percentage of patients who received Invasive mechanical ventilation or died in the dexamethasone group (26%) was lower than that of those in the usual group (27.6%) (rate ratio: 0.93; 95% CI, 0.85–1.01) (Engl 2021). The percentage of patients who were not receiving invasive mechanical ventilation at

randomization and progressed to received invasive mechanical ventilation later was lower in the dexamethasone group than in the usual care group (risk ratio, 0.79; 95% CI, 0.64 to 0.97) (Engl 2021). The percentage of those who were receiving invasive mechanical ventilation at randomization and did not require invasive mechanical ventilation later was higher in the dexamethasone group than in the usual care group (rate ratio, 1.47; 95% CI, 1.20 to 1.78) (Engl 2021). The percentage of the patients who were not receiving renal- replacement therapy (renal dialysis or hemofiltration) at randomization and had to use later within 28 days was lower in the dexamethasone group than in the usual care group (risk ratio, 0.61; 95% CI, 0.48 to 0.76) (Engl 2021).

# 6 VACCINES

There are many covid-19 vaccines in the market, and this paper will focus on three vaccines developed by three renowned institutions -- Moderna, Pfizer/ BioNTech, and Oxford/ AstraZeneca. These companies all had major breakthroughs in COVID-19 vaccine development in 2020. Vaccines developed by these institutions have already been purchased by different governments and used in different countries. They all showed high efficacies for the prevention of original SRAS-CoV-2. However, due to the development of the pandemic and the evolvement of different variants, the efficacies of these vaccines are challenged.

## 6.1 Vaccine Produced by Moderna

Moderna, a biotechnology company, specializes in the mRNA vaccine for COVID-19. It shows that a total of 30,000 people in the United States have participated in its COVID-19 vaccine clinical trial, for which 79.4% are White, 10% are African American, 5% are Asian, and <5% other races/ethnicities (CDC 2021). For the age and sex breakdown of those people, 52.6% are male, 47.4% are female, 25% are 65 years and older, and 75% of people are between 18-64 years old(CDC 2021). According to data published by CDC, most people who participated in the trials (82%) were considered to have an occupational risk of exposure, with 25% of them being healthcare workers(CDC 2021). People in the clinical trials, 22.3% had at least one high-risk condition, which included lung disease, heart disease, obesity, diabetes, liver disease, or HIV infection(CDC 2021). Four percent (4%) of participants had two or more high-risk conditions(CDC 2021). Of the 15,000 vaccinated volunteers, only 11 were infected with the virus, and no one developed severe symptoms(Moderna, Inc. 2020). Among the 15,000 placebo-vaccinated volunteers, 185 were infected with the virus, of which 30 developed into severely ill patients, and one died because of the disease(Moderna, Inc. 2020). It is pointed out in the Moderna's latest vaccine phase III clinical trial data submitted to the FDA that the vaccine efficacy is 94.5% (P<0.0001) (Moderna, Inc. 2020) in preventing infection with Covid-19 and can prevent 100% of the severe symptoms of Covid-19.

By using the genetic information of COVID-19, the sequence of spike proteins in the virus is identified and encoded into mRNA. When humans received the vaccines, the mRNA is taken into immune cells. When mRNA is inside immune cells, the cells use it to make the protein. After the protein is made, the cells break down the mRNA. Next, the cells display these protein pieces on their surface, which allows the immune systems to recognize these proteins and begin building an immune response by making antibodies. These antibodies can prevent the body from getting an infection in the future. The benefit of mRNA vaccines, like all vaccines, is those vaccinated gain this protection without ever having to risk the serious consequences of getting sick with COVID-19. (Figure 4)

## 6.2 General Information about the Injection of Vaccine Produced by Moderna

People receive vaccines in the muscle of the upper arm. Normally they receive two doses, the time of which was a month (28 days) apart (CDC 2021). The vaccine also does not contain eggs, preservatives, and latex(CDC 2021). The vaccine is recommended for people who are more than or equal to 18-year-old (CDC 2021). Also, pain, swelling, and redness were the most common side effects in the arm where people got the injection, and chills, tiredness, and headache frequently happened throughout the rest of the body (CDC 2021). These side effects usually start within the first two days after getting the vaccine (CDC 2021). They might feel like flu symptoms and might even affect people's ability to do daily activities, but normally they will go away in a few days (CDC 2021).

## 6.3 Vaccine Produced by Pfizer/ BioNTech

BioNTech is another company that specialized in the mRNA vaccine for COVID-19. About 82% of people who participated in the research are White, 9.8% are African American, 4.4% are Asian, and <3% other races/ethnicities (CDC 2021). For the age and sex breakdown, 50.6% of the people are male, 49.4% are female, and 21.4% are 65 years and older (CDC 2021). Also, the most frequent underlying medical conditions for those people were obesity (35.1%), diabetes (8.4%), and pulmonary disease (7.8%) (CDC 2021). Among 36,523 participants who had no evidence of existing or prior SARS-CoV-2 infection, 8 cases of Covid-19 with onset at least seven days after the second dose were observed among vaccine recipients and 162 among placebo recipients. This case split corresponds to 95.0% vaccine efficacy (95% confidence interval [CI], 90.3 to 97.6) (Polack et al. 2020). Among participants with and those without evidence of prior SARS CoV-2 infection, 9 cases of Covid-19 at least seven days after the second dose were observed among vaccine recipients and 169 among placebo recipients, corresponding to 94.6% vaccine efficacy (95% CI, 89.9 to 97.3) (Polack et al. 2020). In general, local reactions were mostly mild-to-moderate in severity and resolved within 1 to 2 days. No deaths were considered by the investigators to be related to the vaccine(CDC 2021).

By using the genetic information of COVID-19, the sequence of spike protein in the virus is identified. This sequence is encoded into mRNA. mRNA formulated in LNP enters the cell. When the whole things enter the cell, mRNA is released. Then, spike protein is made and processed. APCs present spike protein fragments, and these can activate the formation of T cells and B cells. The CD8+ cytotoxic T cells can eliminate virus-infected cells and potentially increase the length of protection. The B cells will become virus-neutralizing antibodies. These can bind spike proteins and prevent virus infection of human cells. In addition, the memory T and B cells provide immune memory to ensure long-term protection against the virus.

## 6.4 General Information about the Injection of Vaccine Produced by Pfizer/ BioNTech

People receive vaccines in the muscle of the upper arm. Normally, they receive two doses, the time of which was 21 days apart. The vaccine does not contain eggs, preservatives, and latex(CDC 2021). This vaccine is available for people aged 12 years older (CDC 2021). The side effects of this vaccine are similar to those produced by Moderna.

## 6.5 Information about People Who Cannot Receive mRNA Vaccines, Both Vaccines Produced by Moderna or Pfizer/ BioNTech

People who have severe allergic reactions (anaphylaxis) or an immediate allergic reaction to any ingredient in an mRNA COVID-19 vaccine should not get this mRNA vaccine (CDC 2021). Also, people who have severe or immediate allergic reactions (anaphylaxis) after getting the first dose of the vaccine should not get another dose of this mRNA COVID-19 vaccine (CDC 2021). In both situations mentioned above, a reaction within 4 hours of getting vaccinated, including symptoms such as hives, swelling, or wheezing (respiratory distress), is regarded as an immediate allergic reaction (CDC 2021). In addition, people who are allergic to PEG or polysorbate should not get an mRNA COVID-19 vaccine (CDC 2021). Although polysorbate is not an ingredient in either mRNA COVID-19 vaccine, it is closely related to PEG, which is in the vaccines (CDC 2021). (Figure 4)

## 6.6 Vaccine Produced by Oxford/ AstraZeneca

The vaccine produced by Oxford/ AstraZeneca is a viral vector vaccine. It is announced that the vaccines had average effectiveness of 70.4 percent, which splits into 90 percent in one dosing regimen and 62 percent in the other (NEEDHAM 2020). This came after clinical trials enrolled over 24,000 participants from across the UK, Brazil, and South Africa. Further trials will include 60,000 participants from the United States, Kenya, Japan, and India (NEEDHAM 2020). Viral vector-based vaccines use the body's own cells to produce antigens. In the case of SRAS-CoV-2, spike proteins are antigens. Modified viruses (the vector) are used to deliver genetic code for antigen, so spike proteins found on the surface of the virus are delivered into human cells to instruct the body's own cells to make spike proteins. Then, an immune response can be triggered by producing immune T cells and B cells as the immune system identifies that spike proteins do not belong to the human body. This can prevent the body from being infected in the future.

## 6.7 Advantages and Disadvantages of Different Vaccines

First of all, for safety, all three vaccines mentioned above are safe, which means that these vaccines are non-infectious because the real viruses are not injected into human bodies, and only the formation of spike protein stimulates the response of the immune system.

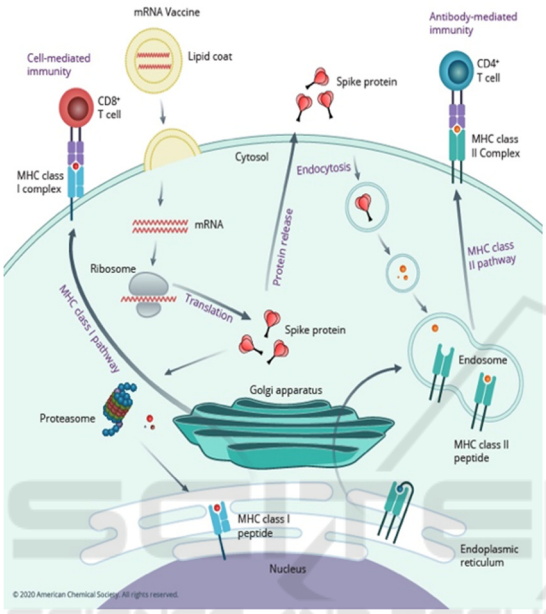


Figure 4: (Worldometer 2022). How do mRNA vaccines work.

For the efficacy, vaccines produced by Moderna and Pfizer/ BioNTech have higher efficacy towards original SRAS-CoV-2, both of which are around 95%(Asipilin 42195 2020) shown in the clinical trial, compared to vaccines produced by Oxford/ AstraZeneca (around 70.4% (Asipilin 42195 2020).

In terms of the efficacy towards different variants, patients who have received a second dose of the vaccines, be it vaccines produced by Pfizer/BioNTech, Moderna, or Oxford/ AstraZeneca, have a higher percentage of preventing infection of the virus (Table 2, Table 3, and Table 4). Vaccines produced by Pfizer/BioNTech (above 90%) and Moderna (around 90%) have higher efficacy towards alpha variant; Moderna's vaccines have higher efficacy when dealing with the beta variant and gamma variant; Oxford's / AstraZeneca's vaccines have lower efficacy when dealing with delta variant compared to that of Pfizer/BioNTech. Other data can refer to Table 2, Table 3, and Table 4 below.

For the production of vaccines, all of them can be produced faster than conventional vaccines because the time to cultivate the virus can be saved. In terms of the distribution of vaccines, vaccines produced by Pfizer/ BioNTech can only store in a fright, which is 2-8°C for five days(Asipilin 42195 2020). However, vaccines produced by Moderna and Oxford/ AstraZeneca can be stored in a fright which is 2-8°C for a long time, which are one month and six months respectively . Normally, the storage temperature for vaccines produced by Pfizer/ BioNTech is -70°C and this for vaccines produced by Moderna is -20°C, and this for vaccines produced by Oxford/ AstraZeneca is 2.22-7.78°C (Asipilin 42195 2020).

In addition, for the price of different vaccines, vaccines produced by Oxford/ AstraZeneca are the cheapest, costing only 3.5USD per dose (Asipilin 42195 2020). Also, vaccines produced by Moderna and Pfizer/ BioNTech cost 35USD and 20USD per dose. It is obvious that vaccines produced by Pfizer/ BioNTech are the most expensive ones (Asipilin 42195 2020).

## 6.8 Other Types of Vaccines

There are two other common types of vaccines in the world: inactivated vaccine and protein subunit vaccine. For inactivated vaccine, the inactivated virus can no longer replicate or reproduce (Johns Hopkins University 2020). The immune system is exposed to viral proteins, but the inactivated virus does not cause disease. Inactivated viruses stimulate the body's immune system to produce antibodies, so when people are exposed to natural viruses, antibodies work to fight the virus (Johns Hopkins University 2020). The production of inactivated vaccines requires the ability to cultivate or breed a large number of viruses. Since the virus cannot replicate outside the host cell, the vaccine virus needs to be cultured in a continuous cell line or tissue (Johns Hopkins University 2020). Several inactivated vaccines are currently widely used, including vaccines against influenza, polio, hepatitis A and rabies viruses. The inactivated virus can no longer replicate or reproduce (Johns Hopkins University 2020). Bharat Biotech is one of the companies which is developing this type of vaccine for COVID-19.

For subunit vaccine, it contains fragments of protein from the pathogen. The protein selected must be likely to produce a strong and effective immune response. In the case of SRAS-CoV-2, spike proteins on the surface are always selected. When these fragments enter our body, the immune system can try to produce immune cells and antibodies to defend

these fragments. As these fragments are incapable of causing diseases, some side effects can be minimized. However, a disadvantage of this vaccine is that the antigens used to elicit an immune response may lack pathogen-associated molecular patterns(Gavi 2021). These patterns can be read by immune cells and recognized as danger signals, so their absence may result in a weaker immune response (Gavi 2021). Also, because the antigens do not infect cells, subunit vaccines mainly only trigger antibody-mediated immune responses, which means the immune response may be weaker than with other types of vaccines (Johns Hopkins University 2020). To deal with this problem, subunit vaccines are sometimes delivered alongside adjuvants, and another booster dose may be required (Gavi 2021). There are also upsides to this type of vaccine. They are cheaper to produce and more stable.

# 7 CURRENT SITUATION OF THE PANDEMIC

Although people can be vaccinated to prevent the SARS-CoV-2, there is no downward trend of the covid cases and death cases indicating the alleviation of the problem. This is due to the emerging of new variants, and the covid vaccines are developed by targeting the original unmutated virus. However, different governments have encouraged residents to get vaccines and have imposed strict policies to prevent the spread of the virus. These actions can potentially lower the risk of being infected.

# 8 CONCLUSION

In conclusion, the spike protein in the SARS-CoV-2 virus is responsible for the transmission of the virus, and different variants arisen because of the mutation of this protein. Also, remdesivir and dexamethasone are the two medicines that are currently used in the treatment, which shows efficacies in shortening the recovery time and lowering the mortality rate. In terms of the covid vaccines, it is clear that all three vaccines are recorded drops in their efficacies because of the emerging of different variants. Therefore, the development of vaccines to deal with different covid variants and prevention of further mutation of the virus are vitally important to fight the virus.

Table 2: A table showing the efficacy of vaccines produced by Pfizer/BioNTech.

| Doses | Severity of illness | Alpha variant | Beta Variant | Gamma Variant | Delta variant |
|---|---|---|---|---|---|
| 1 | Asymptomatic | 38% (29–45%) (Wikipedia 2021) | 17% (10–23%) (Wikipedia 2021) | Not found | 30% (17–41%) (Wikipedia 2021) |
| 1 | Symptomatic | 27% (13–39%) (Wikipedia 2021) | 43% (22–59%) [(Wikipedia 2021) | 43% (22–59%) (Wikipedia 2021) | 33% (15–47%) (Wikipedia 2021) |
| 1 | Hospitalization | 83% (62–93%) (Wikipedia 2021) | 0% (0–19%) (Wikipedia 2021) | 56% (−9 to 82%) (Wikipedia 2021)] | 94% (46–99%) (Wikipedia 2021) |
| 2 | Asymptomatic | 92% (90–93%) (Wikipedia 2021) | 75% (71–79%) (Wikipedia 2021) | Not found | 79% (75–82%) (Wikipedia 2021) |
| 2 | Symptomatic | 92% (90–93%) (Wikipedia 2021) | 88% (61–96%) [(Wikipedia 2021) | 88% (61–96%) (Wikipedia 2021) | 83% (78–87%) (Wikipedia 2021) |
| 2 | Hospitalization | 95% (78–99%) (Wikipedia 2021) | 100% (74–100%) (Wikipedia 2021) | 100% (74–100%) (Wikipedia 2021) | 96% (86–99%) (Wikipedia 2021) |

Table 3: A table showing the efficacy of vaccines produced by Moderna.

| Doses | Severity of illness | Alpha variant | Beta Variant | Gamma Variant | Delta variant |
|---|---|---|---|---|---|
| 1 | Asymptomatic | Not found | Not found | Not found | Not found |
| 1 | Symptomatic | 61% (56–66%) (Wikipedia 2021) | 43% (22–59%) (Wikipedia 2021)] | 43% (22–59%) (Wikipedia 2021) | Not found |
| 1 | Hospitalization | 59% (39–73%) (Wikipedia 2021) | 56% (−9 to 82%) (Wikipedia 2021) | 56% (−9 to 82%) (Wikipedia 2021) | Not found |
| 2 | Asymptomatic | Not found | Not found | Not found | Not found |
| 2 | Symptomatic | 90% (85–94%) (Wikipedia 2021) | 88% (61–96%) (Wikipedia 2021) | 88% (61–96%) (Wikipedia 2021) | Not found |
| 2 | Hospitalization | 94% (59–99%) (Wikipedia 2021) | 100% (Wikipedia 2021) | 100% (Wikipedia 2021) | Not found |

Table 4: A table showing the efficacy of vaccines produced by Oxford/ AstraZeneca.

| Doses | Severity of illness | Alpha variant | Beta Variant | Gamma Variant | Delta variant |
|---|---|---|---|---|---|
| 1 | Asymptomatic | 37% (32–42%) (Wikipedia 2021) | Not found | Not found | 18% (9–25%) (Wikipedia 2021) |
| 1 | Symptomatic | 39% (32–45%) (Wikipedia 2021) | Not found | 33% (26–40%) (Wikipedia 2021) | 33% (23–41%) (Wikipedia 2021) |
| 1 | Hospitalization | 76% (61–85%) (Wikipedia 2021) | Not found | 55% (47–62%) (Wikipedia 2021) | 71% (51–83%) (Wikipedia 2021) |
| 2 | Asymptomatic | 73% (66–78%) (Wikipedia 2021) | Not found | Not found | 60% (53–66%) (Wikipedia 2021) |
| 2 | Symptomatic | 81% (72–87%) (Wikipedia 2021) | 10% (−77 to 55%) (Wikipedia 2021) | 78% (69–84%) (Wikipedia 2021) | 61% (51–70%) (Wikipedia 2021) |
| 2 | Hospitalization | 86% (53–96%) (Wikipedia 2021) | Not found | 88% (78–93%) (Wikipedia 2021) | 92% (75–97%) (Wikipedia 2021) |

# REFERENCES


Asipilin 42195: Comparisons of different advantages and disadvantages of vaccines [Chinese]. Available from: http://mp.weixin.qq.com/s?__biz=MzUzMzkxOTc4NA==&mid=2247485529&idx=1&sn=5ea5d4c26f8ff2d5e7c066f64eb4ab91&chksm=fa9de91ecdea60082b9ab81e29dc34be0b1c53cf6a89dc0973137bd71c224e5992c53bf73f9b#rd (accessed Aug. 18, 2021).

"COVID-19," Wikipedia. Aug. 01, 2021. Accessed: Aug. 18, 2021. [Online]. Available: https://en.wikipedia.org/w/index.php?title=COVID-19&oldid=1036654407

CDC, "Information about the Pfizer-BioNTech COVID-19 Vaccine," Centers for Disease Control and Prevention, Jun. 24, 2021. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/Pfizer-BioNTech.html (accessed Aug. 13, 2021).

"COVID-19 Delta Variant: What You Need to Know." https://www.healthline.com/health-news/the-covid-19-delta-variant-heres-everything-you-need-to-know#What-symptoms-does-the-Delta-variant-cause? (accessed Aug. 05, 2021).

CDC, "Information about the Moderna COVID-19 Vaccine," Centers for Disease Control and Prevention, Jun. 11, 2021. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/Moderna.html (accessed Aug. 12, 2021).

CDC, "Understanding mRNA COVID-19 Vaccines," Centers for Disease Control and Prevention, Mar. 04, 2021. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mrna.html (accessed Aug. 12, 2021).

"COVID Live Update: 206,980,203 Cases and 4,358,550 Deaths from the Coronavirus - Worldometer." https://www.worldometers.info/coronavirus/ (accessed Aug. 14, 2021).

"Dexamethasone in Hospitalized Patients with Covid-19," N. Engl. J. Med., vol. 384, no. 8, pp. 693–704, Feb. 2021, doi: 10.1056/NEJMoa2021436.

I. Kimura et al., "SARS-CoV-2 Lambda variant exhibits higher infectivity and immune resistance," bioRxiv, p. 2021.07.28.454085, Jul. 2021, doi: 10.1101/2021.07.28.454085.

J. H. Beigel et al., "Remdesivir for the Treatment of Covid-19 — Final Report," N. Engl. J. Med., vol. 383, no. 19, pp. 1813–1826, Nov. 2020, doi: 10.1056/NEJMoa2007764.

Johns Hopkins University: Detailed explanation of the types, advantages and disadvantages of the COVID-19 vaccines. [Chinese]. 3 December 2020. Available from: https://mp.weixin.qq.com/s/hWZ0YBL4tgpyB6BaQeVSXQ

"Moderna's COVID-19 Vaccine Candidate Meets its Primary Efficacy Endpoint in the First Interim Analysis of the Phase 3 COVE Study | Moderna, Inc." https://investors.modernatx.com/news-releases/news-release-details/modernas-covid-19-vaccine-candidate-meets-its-primary-efficacy/ (accessed Aug. 08, 2021).

"Moderna COVID-19 vaccine," Wikipedia. Aug. 12, 2021. Accessed: Aug. 14, 2021. [Online]. Available: https://en.wikipedia.org/w/index.php?title=Moderna_COVID-19_vaccine&oldid=1038439218

"Oxford–AstraZeneca COVID-19 vaccine," Wikipedia. Aug. 13, 2021. Accessed: Aug. 14, 2021. [Online]. Available: https://en.wikipedia.org/w/index.php?title=Oxford%E2%80%93AstraZeneca_COVID-19_vaccine&oldid=1038621367

"Page not found (404)," LubioScience. https://www.lubio.ch/blog/neutralizing-antibodies. (accessed Aug. 18, 2021).

"Pfizer–BioNTech COVID-19 vaccine," Wikipedia. Aug. 13, 2021. Accessed: Aug. 14, 2021. [Online]. Available: https://en.wikipedia.org/w/index.php?title=Pfizer%E2%80%93BioNTech_COVID-19_vaccine&oldid=1038650584

R. A. Mansbach, S. Chakraborty, K. Nguyen, D. C. Montefiori, B. Korber, and S. Gnanakaran, "The SARS-CoV-2 Spike variant D614G favors an open conformational state," Sci. Adv., vol. 7, no. 16, p. eabf3671, Apr. 2021, doi: 10.1126/sciadv.abf3671.

"Runtime Error." https://www.who.int/news-room/q-a-detail/coronavirus-disease-covid-19. (accessed Aug. 18, 2021).

"Remdesivir," COVID-19 Treatment Guidelines. https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/remdesivir/ (accessed Aug. 06, 2021).
"SARS-CoV-2 Alpha variant," Wikipedia. Jul. 29, 2021. Accessed: Aug. 04, 2021. [Online]. Available: https://en.wikipedia.org/w/index.php?title=SARS-CoV-2_Alpha_variant&oldid=1036066787
"SARS-CoV-2 Beta variant," Wikipedia. Jul. 28, 2021. Accessed: Aug. 04, 2021. [Online]. Available: https://en.wikipedia.org/w/index.php?title=SARS-CoV-2_Beta_variant&oldid=1035925918
"SARS-CoV-2 Gamma variant," Wikipedia. Jul. 28, 2021. Accessed: Aug. 04, 2021. [Online]. Available: https://en.wikipedia.org/w/index.php?title=SARS-CoV-2_Gamma_variant&oldid=1035998057
"SARS-CoV-2 Delta variant," Wikipedia. Aug. 04, 2021. Accessed: Aug. 04, 2021. [Online]. Available: https://en.wikipedia.org/w/index.php?title=SARS-CoV-2_Delta_variant&oldid=1037048949
"Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine | NEJM." https://www.nejm.org/doi/full/10.1056/NEJMoa2034577?fbclid=IwAR1YoOCQ3DNr0GjMQv4hFXVvu4L8SI0fAMkbJdJdh-AfrLOHBmSVSbo7oTM#.X9QvTNjPnRc.facebook (accessed Aug. 08, 2021).
"Tracking SARS-CoV-2 variants." https://www.who.int/emergencies/emergency-health-kits/trauma-emergency-surgery-kit-who-tesk-2019/tracking-SARS-CoV-2-variants (accessed Aug. 18, 2021).
"The top five coronavirus vaccine candidates explained | WIRED UK." https://www.wired.co.uk/article/coronavirus-vaccines-frontrunners (accessed Aug. 08, 2021).
"What are protein subunit vaccines and how could they be used against COVID-19?" https://www.gavi.org/vaccineswork/what-are-protein-subunit-vaccines-and-how-could-they-be-used-against-covid-19 (accessed Aug. 14, 2021).
Y. Huang, C. Yang, X. Xu, W. Xu, and S. Liu, "Structural and functional properties of SARS-CoV-2 spike protein: potential antivirus drug development for COVID-19," Acta Pharmacol. Sin., vol. 41, no. 9, pp. 1141–1149, Sep. 2020, doi: 10.1038/s41401-020-0485-4.