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Guest Editorial

The Differences between Traditional Vaccines and RNA Vaccines: Safety, Efficacy, Reliability and Future of COVID-19 Vaccines

Mulazim Hussain Bukhari[1], Mobin Syed[2], Shahzadi Zain[3]

[1]Azad Jammu Kashmir Medical College, Muzaffar Abad; [2]Drbeen.com, California, USA; [3]University of Western Ontario, Canada.

Abstract

Vaccines are the most safe, effective and economical mean of controlling Pandemic. Vaccines work by activating the natural immune response of human body. Vaccine manufacturing companies around the world sprang into action as soon as the genetic sequence of the novel coronavirus was shared by the Chinese authorities, early 2020. Moderna of the USA and a joint US-German vaccine from Pfizer-BioNTec, Sinovac, CanSino and AstraZeneca are among the leading names. Messenger RNA (mRNA) is a new approach to develop vaccines for SARS-CoV-2. Traditional vaccines produce the immune response by injecting a killed, or attenuated germ into human bodies. New mRNA vaccine, on the other hand, teaches the human cells to make a protein or even just a piece of a protein, that triggers an immune response inside the human. The mRNA vaccines have several benefits over traditional vaccines such as shorter manufacturing duration, stronger immune response and no post-inoculation viral activation. The traditional vaccine activates only humoral immune response and synthesize antibodies, whereas, mRNA vaccine triggers both humoral and cellular immune response. Traditional vaccines use weakened pathogen that, although rarely, can re-activate to cause infection in severely immune-compromised patients. There is no such danger with mRNA vaccine or recombinant techniques. The FDA has now approved many COVID-19 vaccines for use, so far.

Key Words: COVID-19, SARS Cov-2, Traditional Vaccine, mRNA Vaccine, AstraZeneca, Pfizer-BioNTec, Moderna, CanSino, Sinovac, Sinopharma.

Introduction

The SARS-CoV-2, the causative agent of COVID-19, emerged in China in late 2019. It was declared a pandemic by the WHO in March 2020. It has grasped the entire world in fear, and uncertainty. As of December 2020, COVID-19 has affected roughly 103 million people and killed over 2.5 million people. USA alone has confirmed about 26 million cases so far.[1]

SARS-CoV-2 is a deadly emerging new virus. Countries around the world are trying to outdo each other in discovering and implementing possible preventative, therapeutic and prophylactic protocols to reduce morbidity and mortality associated with this virus. Antiviral, antibacterial, antimalarial and immunoglobulins etc. have been used in treating COVID-19 with variable success rates. Development of the vaccine against COVID-19 is considered to be an indispensable and crucial component of global attempts to control this Pandemic and many companies are trying to manufacture safe and effective vaccine. [2-3]

Vaccination is an effective yet safe way of protecting people against harmful diseases. It uses one's natural defense system to build resistance against specific infections. Vaccines train human immune system to create neutralizing antibodies, just as it does when

it's exposed to an actual pathogen. These vaccines, however, contain only weakened or killed viruses or bacteria, which do not have the capacity of proliferation and cause the disease. Theses vaccines do not put one at risk of any complications. Most vaccines are given by an injection, but some are given subcutaneously (under the skin), orally (like Polio) or sprayed into the nose. Development of safe and effective vaccines may take years. Vaccine manufacturing process consists of several tedious steps which are led by deliberation and quantifiable methodology. Side effects and any adverse consequences are taken very seriously as vaccines have to pass through arduous approval process before they can be marketed. [2-3]

How many types of vaccines are in the market to be used for SARS-CoV-2?

There is a long list of vaccines on the market, some have been approved while others are awaiting approval while others are still in the womb. Various kind of vaccines include mRNA, viral vectors, proteins or killed coronaviruses vaccines. Previously, development of the safe and effective vaccine is proven to be the most efficient and economical means to prevent and control many infectious diseases in the history. More than 100 companies around the world entered an exploratory or preclinical phase of COVID-19 vaccine development early 2020 but only a couple of companies managed to step into clinical trials phase. These include BNT162 (BioNTech/Fosun/Pfizer), mRNA-1273 (Moderna), Ad5-nCoV (CanSino Biologicals), INO-4800 (Inovio, Inc.), LV-SMENP-DC and Pathogen-specific aAPC (ShinzenGeno-Immune Medical Institute), and ChAdOx1 (AstraZeneca/University of Oxford). After successful phase III trials, three of these vaccines were sent to Food and Drug Administration (FDA) of the USA for approval, and few for emergency use, so far (Table 1-3).[4-5]

The whole world is in a state of chaos and is unmistakably more so since second wave of COVID-19 started. Vaccine manufacturing and testing has been expedited to make vaccine available for public use which raise questions on ethical challenges associated with it. One way of accelerating the vaccine manufacturing process is by using non-conventional novel technology to develop vaccine.

In conventional vaccines, the inactivated or live attenuated pathogen (whole or subunit) is inoculated in human body to stimulate natural immune response. In some advance cases recombinant techniques are being used to develop the vaccines by using a vector delivery systems to express antigen of infectious pathogen. For example a mRNA is introduced in the body to induce both cellular and humoral immune responses, production of which is relatively simple and rapid as compared to conventional vaccines. Some companies are using the preparation of proteins while others are using chemicals to attenuated the SARS-CoV-2 virus in the vaccine. (Table 1).[4-8]

Virus Vector Vaccines

Oxford University is partnering with AstraZeneca, a UK and Swedish company, to develop and test the COVID-19 vaccine. It is an Adenovirus vectored vaccine which is derived from chimpanzee, hence called Chimpanzee Adenovirus-Vectored Vaccine (ChAdOx1 nCoV-19) or AZDD1222.

This recombinant adenovirus vaccine was developed using codon-optimized S-glycoprotein and synthesized with a tissue plasminogen activator (TPA) sequence at the end of 5 'The SARS-CoV-2 sequence encoding amino acids (2 to 1273) and the TPA leader was propagated in a shuttle plasmid. Researchers added the coronovirus spike S2 protein gene to adenovirusses derived from these chimpanzees. These adenoviruses are modified in a way that allows virus entry in human cells, but does not let the virus replicate. As a result, Human immune system forms neutralizing antibodies (NAB) which will provide protection against SARS-COV2 in the future. Various phases of its clinical trial were completed in the United States of America, Japan, Russia, Latin America, Brazil, South Africa, and Kenya. Initial data analysis shows 70% effectiveness, however, trial is still in progress with promising potential. (Table1-2) [9-11]

The mRNA vaccine is not new because scientists have been studying laboratory preparations for these vaccines for more than three decades. These mRNA have been studied previously in infections like cytomegalovirus (CMV), rabies, influenza, and Zika viruses endemics. There are 5 steps in preparation of these Virus Vector Vaccines. (Figure 1-3, Table 1-2). [9-14]

Step 1: Adenovirus extraction

Adenoviruses are common DNA (deoxyribonucleic acid) viruses that typically cause cold or flu-like

symptoms. Scientists extract adenoviruses from chimpanzees. These adenoviruses were modified to deactivate some of its genes. The deactivation of its replicative genes result in a modified Adenovirus that can enter the living host cells but cannot replicate inside them. [9-14]

Step 2: Preparation of Recombinant genetic material

SARS-COV-2 is a RNA (ribonucleic acid) virus which is accompanied by reverse transcriptase enzymes to catalyze the transcription of its RNA into DNA. Next step is to combine this transcripted DNA with plasmid DNA. Bacterial plasmid is an extrachromosomal, circular DNA capable of independent replication. A portion of this plasmid is excised to insert the DNA of SARS-Cov-2 spike protein S2, synthesized in vitro, to make a recombinant genetic material. A portion of this plasmid is cut to insert the in vitro synthesized DNA of the SARS-Cov-2 spike protein S2 and produce a recombinant genetic material. It is used as a virus vector to enter inside human cell, and express SARS-COV-2 spikes protein S2 but cannot replicate to make new virus. [9-14]

Step 3: Introduction of Recombinant genetic material in Producer Cells

This recombinant genetic material (SARS-COV-2/Plasmid) is introduced into another cell called the Producer cell. The nucleus of this cell reads the recombinant genetic material and makes mRNA, which sends a message to the ribosomes. This producer cell is now a Genetically Engineered cell which grows an adenovirus shell around them and is capable of synthesizing Spike protein. [9-14]

Step 4: Preparations of Harvested virus

These genetically engineered cells are now introduced into various human cell strains (Figure 1). "Human embryonic kidney 293 cells (HEK 293) were obtained from an aborted male foetus, donated by a mother for research, in 1973. Medical Research Council Cell Line strain 5 (MRC-5) is another approved cell line, obtained from 14 week old aborted Caucasian male foetus, in 1966 and is used as a substrate for vaccine testing. HEK 293 and MRC-5 cell lines are exposed to these genetically engineered cells containing recombinant SARS-COV-2/Plasmid DNA to make sure the adenovirus do not replicate inside human cell line and just signal Spike protein S2 synthesis." After confirming the expression of S2 spike protein, the cell strain is filtered out of the final product and the virus produced from them are harvested separately. [9-14]

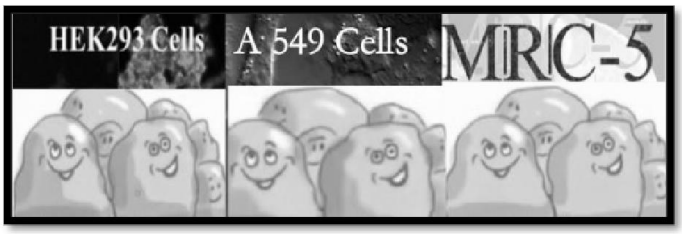

Figure 1: Various human cell lines cells used in mRNA vaccine trials.

Step 5: Mass production of vaccine

Next, these recombinant SARS-COV-2 / Plasmid DNA containing modified Adenoviruses are produced in large numbers and are set up for Clinical trials. Vaccines are developed by training the human body's natural defense system to identify and fight pathogens. It may take up 14 days to develop immuneity after the second dose of AstraZeneca vaccine, and Moderna vaccine and up to 28 days in case of the Pfizer vaccine (Table 1-3). When this vaccine is inoculated in human body, this recombinant DNA/RNA enters human cells, signals mRNA synthesis which in turn signals the ribosomes of human cells to make spikes proteins S2. These S2 proteins are foreign to human body and activates both humoral and cellular immune response. Neutralizing antibodies (NAB) are produced. Therefore, vaccination is a safe and effective way to provoke an immune response in the body without causing illness. Human Immune system is designed to remember previous antigen exposure, naturally. After exposure to one or more doses of the vaccine, the human body usually remains protected from the disease for years, decades, or even life. (Figure 1-3) [15-17]

The Chinese, CanSino vaccine is also based on the recombinant technique of using Adenovirus as a vector. The Russian Ministry of Health has also developed another viral vector vaccine at the Gamaleya Research Institute, called Sputnik V or Gam-COVID-Vac. They used the corona virus spike protein gene in two types of human adenovirus, one called Ed26 and one called Ed5. These adenoviruses

are designed to attack cells without any means of transport. Up to 91% efficacy has been reported in a Phase 3 trial. One type of adenovirus, Ed 26, is used for the first dose, and then 21 days later, Ed 5 is used for the second dose to trigger the immune response.

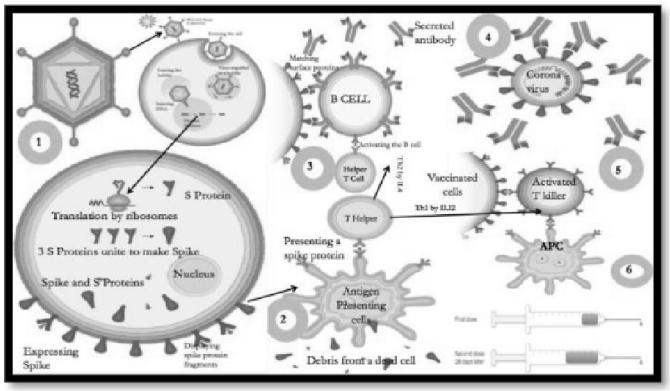

Figure 2: **Showing Mechanism of action of viral vector vaccine. in the in section 1;** adenovirus pushes its DNA of Spike Protein into the nucleus. The adenovirus is engineered so it can't make copies of itself, but the gene for the coronavirus spike protein can be read by the cell and copied into a molecule called messenger RNA, or mRNA. In section 2; presented to T helper cells, through Th1, by IL4 B cells are activated, 3, Neutralizing antibodies (NAB) are made by B cells converting to Plasma cells through IL4. IL5, 4, NAB identify the SARS-CoV-2 and binds to the virus to help immune system to destroy it rapidly, and kill it, on the other hand 5; through IL12, cytotoxic immunity through CD-8 cells, and 6; dosage of Vaccine.

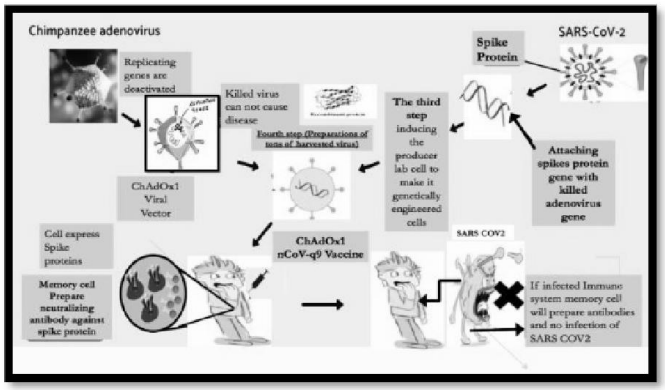

Figure. 3*:* Steps of developing Virus Vector Vaccine using Adenoviruses

Researchers have been working and finding out with mRNA vaccines for over 3 decades now. It is easy to develop the vaccines in a laboratory by using readily available materials. This means the process can be standardized and scaled up, making vaccine manufacturing process way faster than traditional methods of making vaccines. This means that the process can be standardized and extended, making the vaccine production process much faster than traditional vaccine production methods. After the Chinese government provided the required information on SARS-COV-2 in early 2020, scientists began working on the mRNA instructions for cells to use the similar spike protein as SARS-COV-2 in an mRNA vaccine build up. This technique allows the vaccine to be protected against multiple infectious agents simultaneously, thus reducing the number of shots needed for protection from common vaccine-prevent-abledisease-ases.[12-13]

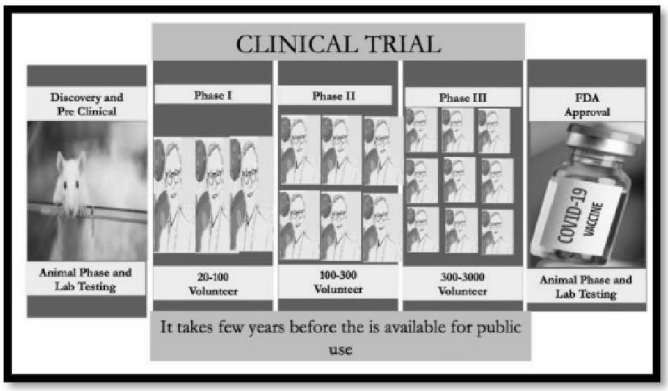

Figure. 4: Standard Vaccine Production Protocol for Infectious Disease.

In traditional vaccines (Figure), pathogens e.g. viruses or bacteria are either killed or weakened to make a vaccine against any disease, by chemical reactions that reduce its ability to cause disease. The traditional vaccine takes years and years to develop before approval. It is passed from Phase I to IV including the animal phase. The mRNA vaccine, was not trialed on animals, due to emergency bases it was recommended after passing trough three phases only on humans. The mRNA on the other hand, uses mRNA as a blueprint that carries the information to the cells to produce different proteins. This technology uses molecules called "messenger RNA" as antigen, whereas, dead or weakened virus plays the role of antigen itself in the traditional vaccine.[12]

The benefits of mRNA vaccine

The mRNA vaccine has several benefits like, shorter manufacturing duration, and potential for triggering

the immune system without entering the nucleus within a short time. The mRNA vaccines can be developed in a laboratory using DNA templates to expedite the vaccine development process. In addition, thses vaccines are prepared using non-replicative viral components that eliminates the chances of post-inoculation viral activation and infection even in severely immune-compromised individuals. Scientists are also exploring the mRNA technology for its prophylactic and therapeutic potential in addition to disease prevention prospects (Figure 5).[10-13]

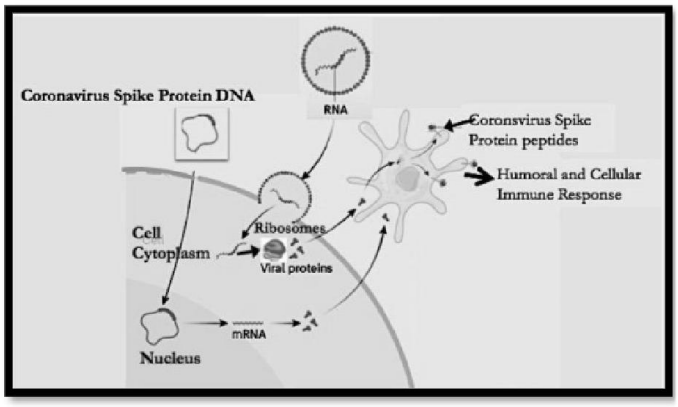

Figure. 5: Mechanism of action of mRNA vaccine to activate innate and adaptive immune system.

Mechanism of Action for mRNA Vaccine?

The mRNA vaccines have strands of genetic material inside the nanoparticles. The nanoparticles protect the mRNA from enzymatic action in the body that would otherwise digest it down.

It helps the mRNA to enter the muscle cells near inoculation site. The mRNA can most easily be described as "Instructional genes for the cell ribosomes on how to make a piece of the spike protein that is similar to the spikes of the SARS-CoV-2".

Since only part of the protein is made, which then unite to make a spike, therefore it does not do any harm to the DNA of the human. It has antigenic properties to produce immunogenicity against the coronavirus. After the pieces of the spikes proteins are made, the human cells break down the remaining and unwanted mRNA strand. These are then disposes them off using enzymes in the cells through macrophages. It is important to understand that the vaccine's mRNA strand never enters the nucleus or affects human's DNA, genetic material. This fact vanishes the misconception or myth that mRNA vaccines are microchips and could control or alter or modify human DNA genetic makeup.[12-15]

The proteins are displayed on the cell surface, and this protein or antigen is identified by innate immune system as "foreign" or "invader". That activates the adaptive immune system to produce antibodies through IL4, IL5 and cytotoxic CD-8 cells through IL12 and IL2. These are called neutralizing antibodies (NAB), which are specific to the SARS-CoV-2 virus. In this way the immune system is primed to protect against future infection by SARS-CoV-2. Following points are important to consider:

1. Through MCH-I, and IL12, IL2, the CD8+ Cytotoxic T-cells are activated to produce mature T cells and memory T cells.
2. Through MCH-II, the macrophages are activated which in turn activates B cells through IL4,and IL5 and also through IL12, IL2, the CD8+ T cells.
3. The B cells mature into Plasma cells, through IL5, which secrete the Immunoglobulins.
4. Some of the B cells transform into memory B cells
5. Whenever there is an actual infection, these hibernating memory T cells are activated and kill the pathogen through cytotoxic action whereas memory B cells immediately start secreting antibodies
6. Through activation of these two cells, human immune system pin the infective virus down before it can cause any damage

What are SARS-CoV-2 Vaccine; mRNA vaccine and how the mRNA was vehicles in the vaccine Inside an Oily Shell?

The genetic material of the vaccine is mRNA, which is transferred inside the oil nanoparticle as an oil shell. Once injected into the deltoid muscle, human cells will read to produce the "S" protein. If the mRNA is injected directly, it will be destroyed by natural human enzymes, therefore, to preserve these small molecules by wrapping them in oil nanoparticles, which can be easily destroyed at room tempe-

rature due to their fragility. To keep Pfizer safe, ***Pfizer*** has designed special dry ice containers, thermal sensors and GPS trackers to ensure transport at-94 F (–70 C). The moderna's-vaccine should be refrigerated and frozen for 4 years upon sending and storing at 4–7° F (–20 ° C).

How the SARS-CoV-2 Vaccine will work after entering the human cell

When the vaccine is injected into the deltoid, the molecule fuses with several cells, and release mRNA. The sequence of this mRNA will be read by human ribosomes and will form spike proteins. These are expressed on the cell surface and taken up by macrophages and eventually destroyed by macrophages, leaving no permanent traces of mRNA molecules. Some of the spike proteins form spikes that move to the surface of the cell and spread through their ends. The vaccinated cells break some proteins into pieces, which they present on their surface. These dispersed spikes and fragments of spike proteins can then be identified by the immune system. Our innate system (an antigen presenting cell) will identify this spike protein debris and present it to naïve T cells, helper T cells can sound the alarm and other adaptive immune B and T cells for infection together Can help bring IL-4 will alert B cells, IL4 and IL5 convert them into plasma cells. Some of the B cells directly and indirectly lock on spike proteins. These cells will start making neutralizing antibody (NAB) against the spike protein and will make mammary cells. NAB can stick to the spikes of the coronovirus, mark the virus for destruction, and prevent infection by blocking the viral spikes from attaching to other cells.

The APCs can also activate another type of immune cell called a killer CD 8+ cells by IL12 and IL2, to seek out these particles and destroy all coronavirus infected cells, which display the spike protein fragments on their surfaces.

Schedule of the doses of the SARS-CoV-2 vaccine, needed to train the immune system. The Pfizer-BioNTech vaccine requires two 0.3 ml injections, 21 days apart, to prepare the immune system well enough to fight the coronavirus. But because the vaccine is so new, researchers aren't sure how long it will take to protect it. A preliminary study found that the vaccine appeared to offer strong protection around 10 days after the first dose compared to people taking a placebo, and full protection after 14 days after the second dose. The dose of Moderna vaccine is the same, but the second dose is given 28 days after the first injection. The number of antibodies and killer T cells may drop several months after vaccination. But the immune system also contains special cells called memory B cells and memory T cells, which can store information about the coronavirus for years or even decades.

How to prepare and administer vaccines using mRNA?

Each vial of vaccine contains 5 doses of 0.3 milliliters. The vaccine should be thawed before injection and diluted with saline solution. Once diluted, the vial should be used within six hours. For Moderna vaccine, each vaccine vial contains 10 doses of 0.5 ml. Before injection, the vials should be warmed to room temperature. Dilution with saline solution is not necessary. (Figure 5)

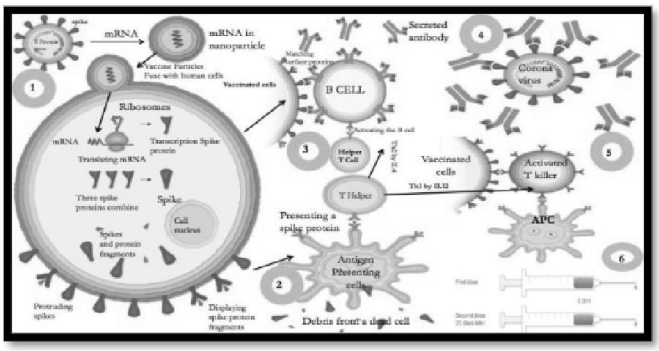

Figure 5: **The mechanism of action of mRNA Vaccine**

Section1 the virus similar mRNA is prepared and saved in nanoparticle, injected in deltoid muscle cells, mRNA enters the cells, translated by ribosomes, Spike proteins are expressed in the cells and taken by the APC, . In section 2; presented to T helper cells, through Th1, by IL4 B cells are activeated, 3, Neutralizing antibodies (NAB) are made by B cells converting to Plasma cells through IL4. IL5, 4, NAB identify the SARS-CoV-2 and binds to the virus to help immune system to destroy it rapidly, and kill it, on the other hand 5; through IL12, cytotoxic immunity through CD-8cells, and 6; dosage of Vaccine.

What is the mechanism of Protein-Based Vaccines

Maryland-based ***NovaVax*** has developed this protein-based coronavirus vaccine ***NVX-CoV2373*** by

sequencing the SARS-CoV-2 spike protein gene. The modified gene was inserted into the baclovirus and allowed to infect moth cells. Researchers have reported that infected moth cells synthesize spike proteins that produce spikes similar to those on the surface of coronaviruses that were successfully cut and separated. These spike proteins were then placed together in nanoparticles that mimic the molecular structure of the coronavirus. This vaccine is reported to produces NAB proteins during the clinical trials in UK, and another one in the USA at the end of December, 2020. The vaccine is expected to activate the innate part of the human immune response. These antigen rendering cells (APCs) break the spike protein into small pieces to display on their surface. The passive helper T cell recognizes these fragments by MCH-2. Once activated by IL-12 and IL-4, they recruit other immune cells to respond to the vaccine by activating cytotoxic CD-8 cells and B cells, respectively. B-cells can also hit vaccine nanoparticles directly. B cells have surface proteins in different shapes, and some may have the right shape to attach to spike proteins. When the B-cell stops, it can pull into the vaccine particle and present spike protein fragments on its surface. Now the B-cell multiplies and releases antibodies that have the same shape as surface proteins. It is based on two doses Base, every 21 days. When acting like a protein-based vaccine against other diseases, it can form specialized groups of cells called memory B cells and memory T cells. These cells retain information about the coronavirus for years or even decades, triggering a rapid counterattack in response to new infections. (Figure 6).

The Novavax vaccine is superior to other vaccines because it can remain stable in the refrigerator for up to 3 months. But scientists are completely uncertain about the duration of protection it offers.

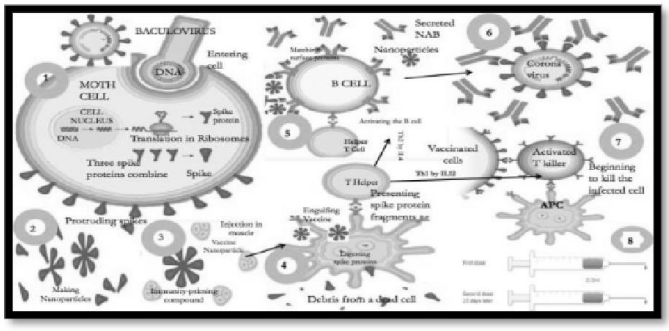

Figure 6: **Mechanism of action of spike Protein Vaccine.**

Section 1,2 A modified spike DNA gene inserted into baculovirus and then to infect moth cells to produced spike proteins that spontaneously joined together to form spikes, Section 3. Injected into the muscles of the arm with many spike nanoparticles which are attracted immune cells to the site of the injection which responds more strongly to the nano-particles. In section 4; APC cells present to T helper cells, through Th1, by IL4 B cells are activated, 5, Neutralizing antibodies (NAB) are made by B cells converting to Plasma cells through IL4. IL5, 4, NAB identify the SARS-CoV-2 and binds to the virus to help immune system to destroy it rapidly, and kill it, on the other hand 5;through IL12, cytotoxic immunity through CD-8cells, and 6; dosage of Vaccine. Note some of the spike nanoparticles are directly taken by B cells to make NAB,

What is the mechanism of inactivated Coronavirus Vaccines

Sinopharm Group, and ***Sinovac Biotech*** are among the companies that used technology to attenuated (Inactivated) of SARS-Co-2 virus to make vaccines. ***Sinophorm*** Group's BBIBP-core vaccine is approved for emergency use in China, Bahrain, and the United Arab Emirates. They claim an effectiveness rate of 79.34%. **Sinovac** Biotech's candidate vaccine, ***CoronaVac***, is licensed for limited use in China. Brazilian tests showed an overall effectiveness of more than 50 percent, the minimum threshold for authorization of the coronavirus vaccine by many regulatory agencies. Although India Biotech's ***Covaxin*** vaccine is licensed for emergency use in India, the results of the Phase 3 trial have not been published. The effectiveness of the vaccine is not yet known. (Figure7) Candidates for this vaccine are based on inactivated coronavirus. They work without the risk of a severe disease response by using the dead viral particles to expose the body's immune system to the virus. This is a traditional approach to vaccine synthesis that has been used with success in many known vaccines such as rabies.

Moderna and Pfizer, on the other hand, are mRNA vaccines, which means that a part of the genetic code of the coronavirus is injected into the body and activates the body. Starting to make viral proteins, but not all of the virus, is enough to train the immune system to attack.

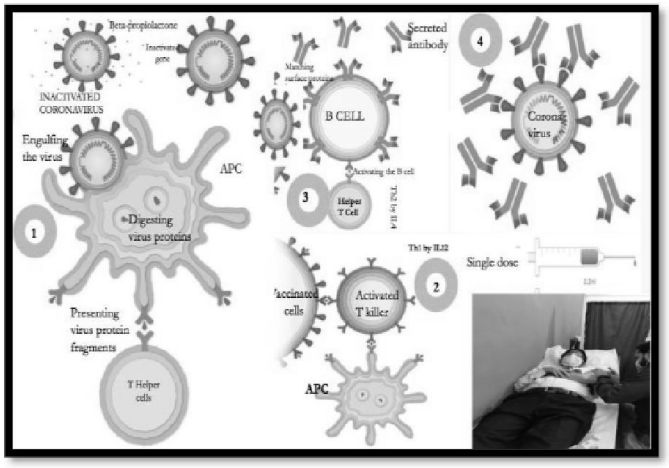

Figure 7: **Mechanism of action of inactivated viral vaccine.**

Section 1, the coronaviruses was harvested and adjuvant aluminum ($Al\text{-}OH_3$) was added after filtering the harvested viruses through 0.22 µm, and inactivated with a chemical called beta-propiolactone which disabled the coronaviruses gene for replication but their proteins, including spike, remained intact. Section 2. Injected into the muscles of the arm which are attracted immune cells to the site of the injection. In section 3; APC cells present to T helper cells, through Th1, by IL4 B cells are activated, 5, Neutralizing antibodies (NAB) are made by B cells converting to Plasma cells through IL4. IL5, 4, NAB identify the SARS-CoV-2 and binds to the virus to help immune system to destroy it rapidly, and kill it, on the other hand 5; through IL12, cytotoxic immunity through CD-8cells, and 6; dosage of Vaccine. Note some of the inactivated coronavirus are directly taken by B cells to make NAB,

Comparison of various vaccines

A sense of frustration is developing in the medical world over lack of uniformity in safety and effectiveeness data released by various vaccine manufacturing companies. Pfizer-BioNTec and Moderna have claimed over 90% efficacy results. AstraZeneca/Oxford University have released multiple data points for its vaccine efficacy but have shown promising results recently. Overall, Moderna, Pfizer and AstraZeneca have revealed encouraging safety and efficacy data in recent weeks (Table 1-2). [13-16]

Pfizer-BioNTec COVID-19 vaccine was approved first in UK and then authorized by FDA in December 2020 for emergency use. Moderna COVID-19 vaccine was approved next. Clinical trials of both of these vaccines have shown encouraging safety profile with only minor side effects reported post-vaccine. No serious adverse effects, hospitalization or mortality were reported. Significant positive immune response was reported in an interim analysis of clinical trials.[15-16]

Pfizer-BioNTec and *Moderna COVID-19* vaccine require ultracold (-75 °C) and freezer (-8 °C) temperature, respectively. ***AstraZeneca COVID-19*** vaccine can be stored, transported, and handled between 2°C to 8 °C for at least six months in lab-grade refrigerator conditions. Therefore, it will have a significant supply advantage over Moderna and Pfizer/BioNTec and will be beneficial for low resource settings such as rural America and the developing countries. As AstraZeneca move closer to approval and authorization for emergency use in Pandemic, they are ready to roll out over 3 billion dose of vaccines in 2021. [15-17]

These vaccines are safe and their side effects are reported to be minor such as a pain or redness at the injection site, or low-grade fever and these symptoms are temporary. Mild reactions or adverse effects subside within a few days without any medical intervenetion. Manufacturing companies and authorization agencies continue to do post-marketing surveillance and monitoring for vaccine safety profile, and to detect any rare adverse events that did not surface during clinical trials.[15-17]

CDC Recommendation

FDA of the USA has approved and authorized two vaccines for interim or emergency use, so far. As these vaccines roll out for public use, the Centre of Disease Control and Prevention (CDC) has an important role to play in clarifying the misconceptions regarding the vaccine, to increase its acceptability and uptake. CDC website is updated regularly to inform medical community and general public about vaccines, its safety and effectiveness, possible side effects, and eligibility criteria for recipients, in addition to preventative public health measures, on regular basis. [13]

Table 1: *Comparison of the vaccines with available data.* [15-17]

Manufacturing Company, Vaccine name	Type of antigen/ Vector	# Doses, Schedule, Immune Response	Data for COVID-19 Disease			
			Total number of volunteers	Disease in Vaccine group	Severe disease in Vaccine group	Disease in Placebo group	Sever Disease in Placebo group
Pfizer-BioNTech, BNT162b2	mRNA lipid particle	2 doses, 21 days apart, full Immunity after 28 days	43,000	14	0	185	30
Moderna, mRNA-1273	LNP-encapsulated mRNA lipid particle	2 doses, 28 days apart, full Immunity after 14 days	30,000	8	1	162	9
AstraZeneca/ University of Oxford, ChAdOx1 nCoV-19 or AZDD1222	Non-replicating Adenovirus Recombinant tech	2 doses, full doses 28 days apart and full Immunity after 14 days	23,000	Data not confirmed	131	Data not confirmed	Data not confirmed

Table 2: *Comparison Different vaccines in the Market.*[15-17]

Manufacturing company, Doses	Type of antigen/Vector	IM Doses, Schedule	Efficacy	Protection	Storage temperature, Stability duration at room temperature	Price
Pfizer-BioNTech 50 million dose in 2020, 1.5 billion doses in 2021	mRNA lipid particle	2 doses, 21 days apart	95% after 28 days of second dose	Against all variants including delta	-70 ^{0}C to -80 ^{0}C (-94^{0}F) 33 days at room temperature and 6 month at -4C^0	37 USD
Moderna, 20 million dose in 2020, 1 billion doses in 2021	LNP-encapsulated mRNA lipid particle	2 doses, 28 days apart	95% after 14 days of second dose	Against all variants including delta	-4 ^{0}C to -8C^0 (24^{0}F) 6 months	36 USD
AstraZeneca ChAdOx1-S University of Oxford/AstraZeneca	Non-replicating Adenovirus Recombinant tech	2 doses, 14 days apart	70-90% after 14 days of second dose	Against all variants including delta	4 to 8C^0 (39.2F^0)	7 USD
CanSino Biological Inc./Beijing Institute of Biotechnology,	Non-Replicating Adenovirus Type 5 Vector	1 dose	90% after 28 days	Against alpha variants	4 to 8C^0 (39.2F^0)	14-15 USD
Gamaleya (SputnikV) Gamaleya Research Institute,	Non-Replicating Genetically modified)	2 doses, 21 days apart	92% after 14 days second dose	Against all variants including delta	Regular fridge temperature	20 USD

300 million doses	Adeno-based (rAd26-S + rAd5-S)					
Sinovac Biotech's China, 400 million doses	Inactivated Virus	2 doses, 14 days apart	90% after 14days of second dose	Against alpha variants	2 to 8 ^{0}C (36°-46°F)	29 USD
Novavax (Covovax), NVX-CoV2373 100 millions	Protein sub-unit	2 doses, 21 days	96%after 14 days of second dose	Against all variants including delta	2 to 8 ^{0}C (36°-46°F)	32 USD
Johnson & Johnson in 100 millions	Ad26COVS1	Single dose	52-74.4% after 14 days of second dose	Against all variants including delta	Not available	10 USD

Table 3: *Comparison Different vaccines in the Market.*[15-17]

Name of vaccine with company and doses	**Moderna**	Pfizer-BioNTech
Type of Vaccine	mRNA	mRNA
Preservative	Nil	Nil
Adjuvant/Antibiotic	Nil	Nil
DNA Change	No	No
Immunogen/Antigen	Spike protein	Spike protein
Allergic reaction reported	No	Yes
Efficacy	>94%	>94%
Storage	Freezer-20C^{O}	Ultra-cool-75C^{O}
Life in refrigerator	30 Days	5 days
Transport	Freezer	Cold chain/dry Ice
Dosage	100ug x 2 doses	100ug x 2 doses
Interval	28 days	21 days
Efficacy start	14 days after 2nd dose	28 days after 2nd dose
Age	≥18 years	≥16 years
Usage	Started	Started
Sites	Multiple	Few
Infertility as S/E	No	No
Safe in pregnancy	6 Pregnancies	12 Pregnancies
Infection (Vaccine/Placebo group)	5/90	8/162
Sever (Vaccine/Placebo group)	0/11	¼
Death (Vaccine/Placebo group)	0/1	0/0
Previously COVID-19	340/334	1/1
Stop transmission	Unknown	Unknown

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