SIR P. T. SARVAJANIK COLLEGE OF SCIENCE
DEPARTMENT OF PHYSICS

SPECTRUM

Special Issue, December-2020

COVID-19

The Vaccine Challenge

Editorial

The last issue of Spectrum (April & August 2020) was dedicated to Corona Virus (SARS-CoV-2) as it has changed our habits, our routines, human relationships, and small everyday gestures. We had difficult days, made even more difficult by the alarmists and the spread of fake news. The idea of the preceding issue was to spread awareness and at the same time provide quality scientific information to understand the virus and conferred precautions need to stop the spread of it. This issue continues the legacy to disseminate the recent advancement in the field of development of mRNA vaccines, its effectiveness, and mutation of the SARS-CoV-2. All the three articles in this issue were written with great details by our beloved, Dr. Pruthul R Desai, Principal, Sir P T Sarvajanik College of Science, Surat. While jotting down these articles, he ensured that the information provided in this issue of Spectrum is reliable, scientifically relevant, and up-to-date. Messenger RNA (mRNA) vaccines, a cutting-edge approach that uses genetically engineered RNA to generate a protein that itself safely prompts an immune system. In the first article of this issue, Dr. Desai elucidate about "What is mRNA vaccine, exactly?". It also explains that when we inject the vaccine into the body, how it will interact with the cell and trigger our immune system. It also clarifies that "Is it safe?" and at the same time help us to reach the "Herd immunity"? In the end, it also conferred challenges associated with the development of the vaccine. The initiation of vaccination has been considered as the beginning of an end of the pandemic. Dr. Desai, in the second article, discusses the working of "Oxford-AstraZeneca Vaccine, and will it be a Game Changer?". The inferences of the vaccine for the deprived countries and the challenges we face in vaccinating the population of the world at large were also discussed. It's a matter of debate nowadays that whether the mutation will affect the efficacy of the vaccines or not. In the third article, the details of the latest mutation found in England are discussed by Dr. Desai. He also discussed in detail, the factors affecting the efficacy of the vaccine on the mutation of the virus.

We hope you will enjoy this collection of articles. We look forward to hearing from you! Your valuable feedback can be sent on ptscsphy@gmail.com

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1. mRNA Vaccine: Is it a Silver Bullet?

Dr. Pruthul Desai

The COVID-19 pandemic has ravaged the world in a short span of eight months and completely changed the way we live. The advent of mRNA based vaccines in record breaking time have raised hope that the scourge of the virus could be tamed soon. In this article, an in-depth analysis of the mRNA vaccine and the factors affecting its efficacy is discussed. The challenges faced in vaccinating the population of the world is also discussed.

1.1 Introduction

COVID-19 has unfurled its tentacles engulfing the entire globe at a breathtaking speed. Humans - the most advanced species on the Earth, have been strung by a very humble assailant which barely measures a billionth of a meter in diameter. The sweeping virus has sent shock waves across the worldwide economic framework and derailed global economic train by siphoning off trillions of dollars, forced many to take perilous journey to their homeland, left a sizeable population distraught and in a state of nervous excitement and has held us hostage from leading our normal life. The year 2020 has truly been, as the Queen Mother once memorably said, an *annus horribilis*!

Since the outbreak nearly a year ago, the humanity has been yearning for a quick fix solution which will bring down the curtains on the COVID-19 pandemic. Vaccine - a purported panacea, typically requires years of research and testing to develop before reaching the clinic for public use. In a major breakthrough, just nine months into the pandemic, the United Kingdom cleared a vaccine developed by US pharma giant Pfizer in collaboration with the German firm BioNTech, for mass vaccination of its population. The first doze of vaccine prepared by Pfizer was administered to an octogenarian lady in London on December 8, 2020.

The pandemic seems to have triggered an unprecedented burst of innovation in vaccinology and nearly fifty different vaccines are out in the pipeline. The World Health Organization (WHO) says that nearly 200 vaccines are under different stages of trial and some of them are most likely to pass through the stringent regulations for “approving" a vaccine. One thing is for sure, the antidote to get rid of this raging pandemic is certainly on the anvil in the coming months.

The record breaking time in which vaccine has been developed underscores the enormous global effort to find one. Whether it was about sharing the DNA sequence of the virus or the sharing experience of handling it, we have never ever witnessed such a synergic cooperation and strong partnerships between scientists, governments, pharma companies, private donors

etc. at the global arena, in the past. This to my mind is one of the notable positives that we could take from this pandemic.

Though the discovery of the vaccine is touted as the beginning of an end, the lightning speed with which this astonishing feat has been achieved has given rise to a cohorts of skeptics. Some of the moot questions are: Whether the pharmaceutical companies have cut corners in developing these vaccines so quickly? Will the vaccine work? How long will the potency of the vaccine last? How long will it take us to vaccinate the whole world?

It is too early to have a definitive answer to the vaccine conundrum. But looking to the revolutionary technology which created the vaccine and an understanding of the principle behind the working of the vaccine will help us to answer some of the questions raised above, though not completely.

1.2 What is mRNA vaccine, exactly?

Vaccines work by training the body to recognise and respond to the proteins produced by disease-causing organisms, such as a virus or bacteria. Traditional vaccines work by injecting a dead or weakened form of the pathogen into the body in preparations that are designed not to make you sick but rather to provoke the immune system into mounting a response.

Unlike conventional vaccines, which are produced using a killed or weakened viruses or snippets of viral proteins, RNA vaccines are constructed using only the pathogen's genetic code. In other words, instead of having the viral protein injected, a person receives genetic material – messenger RNA (mRNA) – that encodes the viral protein. mRNA is like the sticky note you use to jot down a recipe from a friend's cookbook—her cookbook belongs in her house, but you could copy its instructions to help make your dinner [2].

The mRNA is a molecule that essentially puts DNA instructions into action. mRNA sequence is used as a template to build proteins. These proteins are solitary and therefore do not assemble to form a virus. The immune system then detects these viral proteins and starts to produce a defensive response to them [2].

The mRNA vaccines never touch our DNA, and as a result can't interfere with human genes. This unique feature, therefore, makes mRNA vaccine safe with minimal side-effects. "Injecting RNA into a person doesn't do anything to the DNA of a human cell," Jeffrey Almond, a microbiologist at the University of Oxford, told the BBC.

Moderna's vaccine can be stored long-term only at minus 4 degrees Fahrenheit, while Pfizer/BioNTech's needs long-term storage at minus 94 degrees Fahrenheit, reports Umair Irfan for Vox. Messenger RNA is constantly under the threat of being destroyed by other molecules in the envi-

ronment. To prevent any damage, vaccine producers not only make chemical changes to the synthetic mRNA wrapping it in a protective layer, but also store it at the low temperature to trap chemical reactions in slow-motion [3].

“Everything happens more slowly as you lower the temperature," says Margaret Liu, a vaccine researcher and the chair of the board of the International Society for Vaccines. “So your chemical reactions — the enzymes that break down RNA — are going to happen more slowly."

1.2.1 The Spike Protein of SARS-CoV-2

The spike protein of corona virus causing COVID-19, forms the club-shaped protrusions that stick out all over the ball and a longer, thinner stalk, as shown in the fig.(1), resembling a crown or the sun’s corona - hence the name. These spike proteins provide the key target for potential vaccines and treatments to work.

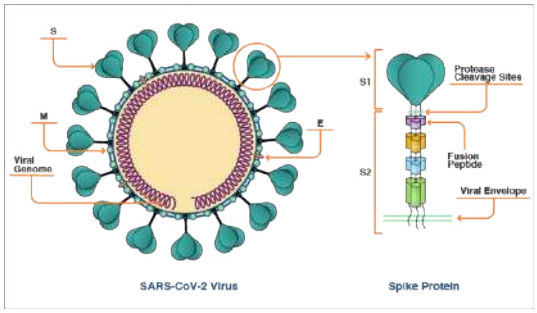

Figure 1: Viral spike protein structure
(Source: https://www.cas.org/blog/covid-19-spike-protein)

Both Pfizer-BioNTech and Moderna vaccine are based on the virus’s genetic instructions to building the spike protein.

1.2.2 mRNA in a Protective Sheath

Messanger RNA (mRNA) is a genetic material which our cells read to produce proteins. mRNA is inherently fragile and rickety. If injected directly into the human cells, mRNA could easily be chopped into pieces by the natural enzymes present in the cell. To prevent this catastrophic breakdown, mRNA is encapsulated by a protective sheath made up of lipid nanomolecules, as shown in the fig.(2).

Even though it is armed with protective covering of lipid nanomolecules, the mRNA capsule will fall apart at room temperature. Therefore, the vaccine should be kept at a very low temperature to prevent any degradation.

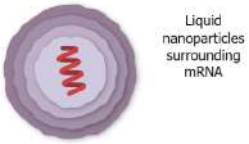

Figure 2: mRNA encapsulated by lipid nanomolecules
(Source: https://www.nytimes.com/interactive/2020/health/pfizer-biontech-covid-19-vaccine.html)

1.2.3 Entering the Cell

On injecting into the upper arm, the vaccine bumps into the human cells and fuses with them, releasing mRNA where it runs into ribosomes - the cell's protein factories. Ribosomes read off the recipe carried by the mRNA, using the cell's tools to assemble a string of amino acids that ultimately become a viral protein directly in the body, as shown in the fig.(3).

This approach mimics what the SARS-CoV-2 does in nature – but the vaccine mRNA codes only for the critical fragment of the viral protein. This gives the immune system a preview of what the real virus looks like without causing a disease [1].

The mRNA from the vaccine is eventually destroyed by the cell, leaving no permanent trace. Some of the spike proteins form spikes that migrate to the surface of the cell and stick out their tips. The vaccinated cells also break up some of the proteins into fragments, which they present on their surface. These protruding spikes and spike protein fragments can then be recognized by the immune system [2].

1.3 The Triggering of the Immunity System

The protein fragments are detected by the immune cells called an antigen-presenting cells, as shown in the fig.(4). The spikes protruding out from the cell's surface are detected by the T-cells. There are two main types of T-cells: helper T-cells and killer T-cells. Helper T-cells stimulate the B-cells to make antibodies and help the killer cells to develop. The killer T-cells directly kill cells that have already been infected by a foreign invader. The T-cells also use cytokines as messenger molecules to send chemical instructions to the rest of the immune system to ramp up its response.

Other immune cells, called B-cells, may bump into the coronavirus spikes and protein fragments on the surface of vaccinated cells. A few of the B-cells may be able to lock onto the spike proteins as shown in the fig.(5). If these B-cells are then activated by helper T-cells, they

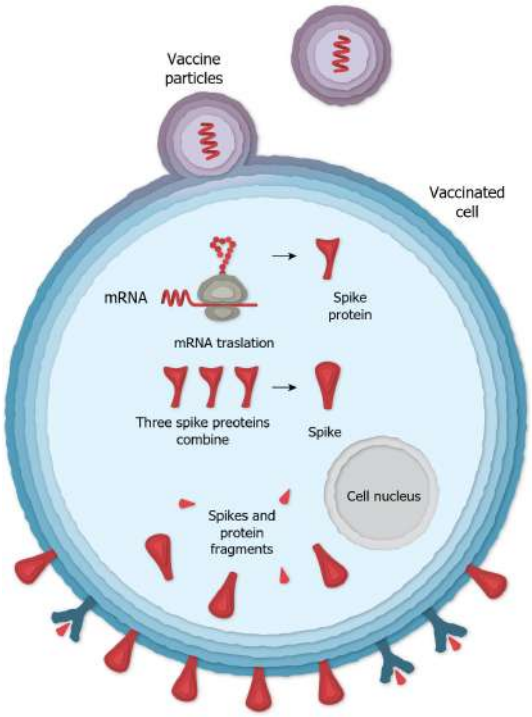

Figure 3: mRNA's entry into the cell
(Source: https://www.nytimes.com/interactive/2020/health/pfizer-biontech-covid-19-vaccine.html)

will start to proliferate and pour out antibodies that target the spike protein [2].

Further reinforcement of the army of the cells to fend of viral attack is brought in by the killer T Cells. The antigen presenting cells activate and trigger killer T Cells which destroy the any corona-infected cells that have been turned into virus making factories as shown in the fig.(6).

1.4 Is it Safe?

The Pfizer-BioNTech vaccine was claimed to be 95 % effective. During the clinical trials, the vaccine was found to be highly effective at reducing cases of symptomatic illness among those who were vaccinated. It requires two jabs separated by an interval of 21 days as shown in the fig.(7). The second and booster dose helps the immune system to retain its memory about the viral proteins for a longer period of time. But because the vaccine is based on new technology, the researchers are wary about speaking out on the time frame for which its efficacy would last.

It's not yet clear how often people will need to be vaccinated for Covid-19. An ideal vaccine

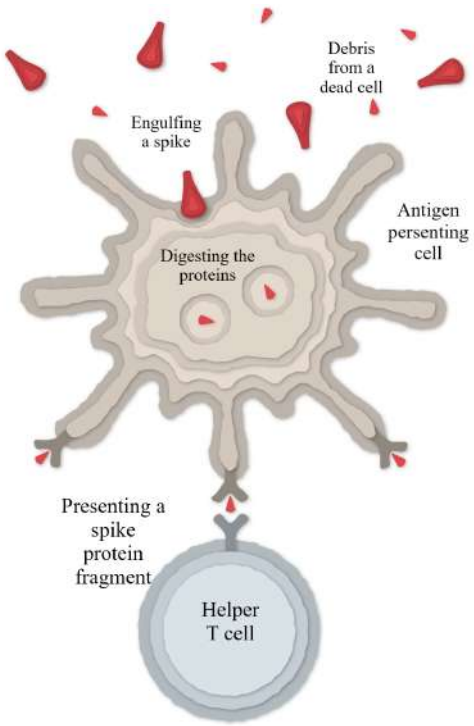

Figure 4: Antigen-presenting Cell and the T-cell
(Source: https://www.nytimes.com/interactive/2020/health/pfizer-biontech-covid-19-vaccine.html)

is supposed to last lifetime. But in practice, it is observed that there are two main causes for tapering off in its efficacy. First, the antigen levels in the body decline over time and second, the strain of the virus may mutate. In the case of SARS-CoV-2, we are unsure how fast it mutates. We can, therefore, hope that the virus is languid and truly reluctant to mutate.

1.5 Will the Vaccine Help in Reaching Herd Immunity?

A vaccine's efficacy matters when it comes to ending a pandemic. Herd immunity has been a buzzword since the pandemic began, but misunderstanding what herd immunity is and how it can be achieved has been just as prevalent. Briefly, herd immunity, or community immunity, refers to having enough people in a population who are immune to a specific disease that the disease has trouble spreading much in that population. To reach herd immunity — the point at which an outbreak peters out — a vaccine must reduce the number of viral spreaders or the pool of people those spreaders can infect, or both.

The pandemic can be sustained only when an infectious person can walk into a place like a

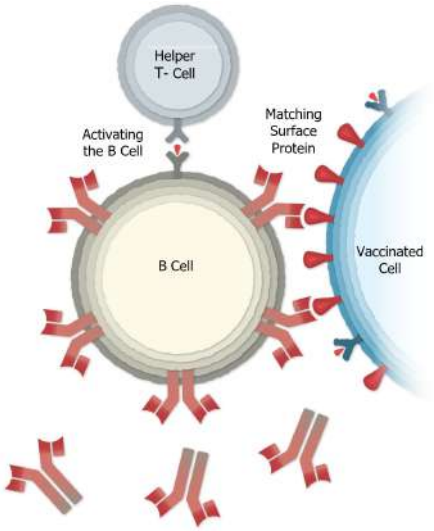

Figure 5: Activating the B Cell
(Source: https://www.nytimes.com/interactive/2020/health/pfizer-biontech-covid-19-vaccine.html)

bar or a gym and find at least one new victim to infect. Eliminate the supply of potential new victims by vaccinating them all, and the virus can go nowhere [3]. Eliminate the supply of spreaders, and you may slow the pandemic even faster.

With the rapid spread of COVID-19 – and high levels of existing infection – the proportion of world population that needs to be vaccinated is high and that is one of the biggest challenges to reach herd immunity.

1.6 Logistical Challenges

Although one advantage of mRNA vaccines is that they're potentially faster to develop than traditional vaccines, their administration and distribution is far more complicated. For example, the 21-day separation has raised some concerns about the patient compliance needed for vaccines to work.

We'll need glass vials and syringes to administer a vaccine, an organised air freight network to delivery doses, as well as cold storages. Each dose of the vaccine must be super-chilled — to minus 70 degrees Celsius — in order to remain effective. "Those types of storage and distribution conditions mean that traditional methods of distributing medicines through pharmacies or normal hospital conditions is simply not viable," says Duncan Matthews of Queen Mary University of London. "The infrastructure needs to be there." Vaccine's immediate impact will

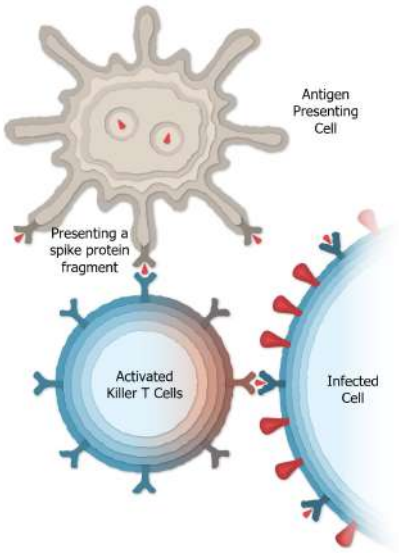

Figure 6: Killer T-cell
(Source: https://www.nytimes.com/interactive/2020/health/pfizer-biontech-covid-19-vaccine.html)

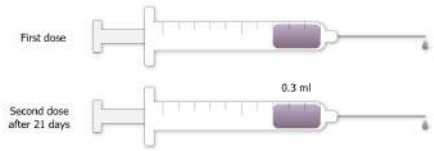

Figure 7: Two doses
(Source: https://www.nytimes.com/interactive/2020/health/pfizer-biontech-covid-19-vaccine.html)

be held back by the insufficient refrigeration facilities available in the most parts of the world and poses a huge challenge for a country as populated as India.

Another very important factor is the ethical quandary. Who gets a shot first? There is a looming roadblock: Some of the rich countries like the US and UK have staked claim on the Pfizer-BioNTech vaccine and have reserved a lion's share for their own. This so called "vaccine nationalism" does not augur well for the eradication of the virus. Unless there is a global agreement, the equitable distribution of the vaccine appears a distant dream. This leaves the poorer nations at peril.

It can hardly escape our attention that the complete eradication of the virus is a distant mirage and only the time will tell when it actually materializes. Till then, we must take all the precautions necessary, particularly in the months going forward, such as washing hands regularly and

wearing masks in public.

1.7 Conclusion

Both the Pfizer-BioNTech and Moderna vaccines called mRNA vaccines, were created using a new method that combines genetic engineering and immunotherapy. Once proven and established, these mRNA vaccines "platforms" promise to come to the rescue far more quickly than predecessors. As soon as scientists can genetically sequence new pathogens, they can start determining the mRNA required to build key proteins within them. This means that future vaccines could be produced on the same rapid time line as Pfizer-BioNTech Covid-19 vaccines.

Sadly, although the current pandemic has made the fact of our global interdependence clear to everyone, it appears that the poorer populations continue to lose out. A concerted global efforts bereft of any possible unfairness is the only way ahead. A failure to do so would place us all at peril. If our past experience is the thing to go by, then it is cause of alarm for the entire human race!!!

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2. Oxford-AstraZeneca Vaccine: Will it be a Game Changer?

Dr. Pruthul Desai

The COVID-19 pandemic has held us hostage from living our normal life and every passing day is excruciatingly taxing on human psyche. The advent of vaccine has been touted as the beginning of an end of the pandemic. But the road ahead is slippery and warrants utmost care. In this article, working of the Oxford-AstraZeneca vaccine has been explained. The implications of the vaccine for the poor countries and the challenges we face in vaccinating the population of the world are also vividly discussed.

2.1 Introduction

With much of the globe in the throes of the COVID-19 pandemic, most of the human population is facing one of the greatest challenges ever. The breathtaking speed at which the number of COVID-19 cases swelled to dizzying heights, triggered an unprecedented global race to develop vaccine - a purported antidote, which we dearly hope, would bring down the curtains on the messy COVID-19 saga. We - the humans, were true to the maxim: 'one brings out one's best when the back is to the wall.' We could develop a vaccine for SARS-CoV-2 virus with remarkable efficacy in a short span of eight months - a remarkable feat indeed. Having a vaccine is an important and decisive step towards attaining the ultimate goal of eradicating the traces of virus from the Earth. Yet, our past experience tells us that merely having a vaccine is woefully inadequate. Ensuring the equitable world wide distribution of the vaccine is vital too.

A number of players were in fray to develop the vaccine for the SARS-CoV-2 virus. The pharmaceutical giants like Pfizer-BioNTech, Moderna, Oxford-AstraZeneca were the front runners in this race for glory and ultimate redemption. Pfizer-BioNTech were first to complete their clinical trials and United Kingdom (UK) was the first country to use the Pfizer-BioNTech vaccine for the mass inoculation of its citizens.

The Pfizer-BioNTech and Moderna vaccines use the messenger RNA (mRNA)- a fragile and rickety molecule which encodes the viral genetic code, to spur the immune response. On the flip side, the mRNA vaccine must be stored at an ultra cold temperature. For example, Pfizer's vaccine must be stored at the ultra-cold temperatures of minus 70 degrees Celsius (-94 Fahrenheit). Once thawed, it can only be refrigerated for 5 days. Moderna's vaccine can be stored at the standard freezer temperatures of -20 Celsius (-4 Fahrenheit) for up to six months. After it's thawed, it can be kept in a refrigerator for up to 30 days.

The COVID-19 pandemic has inflicted the worst social and economic blows on the poor coun-

tries. Their economy is currently in doldrums. A costly vaccine will only compound to their woes. The prohibitive cost of the storage requirements for the mRNA based vaccines would further push back the economic recovery leading to precariously hopeless situation. Poor countries, which contain sizeable percentage of the world population, yearn for an elixir - a cost effective vaccine which could be less taxing on their economy. Oxford-AstraZeneca's vaccine is likely to be the answer to their prayers.

For the sake of humanity, the rich countries should generously dole out dollars from their coffers for the equitable distribution of the mRNA vaccines. Sadly, our experience of yesteryear, presents a gloomy picture and the prospect of the rich countries exhibiting magnanimity are bleak. Yet, we should not be despondent and loose hope.

Seventy-six wealthy nations are now committed to joining a global COVID-19 vaccine allocation plan, co-led by the World Health Organization (WHO) that aims in helping in buying and fairly distributing the shots. COVAX is designed to discourage the national governments from hoarding COVID-19 vaccines and to focus on vaccinating the most high-risk people in every country. Its backers say this strategy should lead to lowering of the cost of the vaccine for everyone and a swifter end to the pandemic. Only time will tell whether the human race rises above its petty squabbles to share resources and vaccines so that the poorest of poor is not deprived of it.

It is too early to have a definitive answer to the vaccine conundrum. But looking to the revolutionary technology which created the vaccine and an understanding of the principle behind the working of the vaccine will help to quell any apprehensions that we may have on the claimed efficacy and safety. Let us have a sneak peek at the working of the Oxford-AstraZeneca vaccine.

2.2 What is Adenovector Virus Vaccine, Exactly?

Vaccines work by training the body to recognise and respond to the proteins produced by disease-causing organisms, such as a virus or bacteria. Traditional vaccines work by injecting a dead or weakened form of the pathogen into the body in preparations that are designed not to make you sick but rather to provoke the immune system into mounting a response.

Unlike the Pfizer-BioNTech and Moderna vaccines which are based on injecting messenger RNA (mRNA) that encodes the viral protein - a radically new approach, the Oxford-AstraZeneca vaccine is more in line with the traditional vaccine. In contrast to the Pfizer-BioNTech and Moderna vaccines which use the single strand RNA to store genetic information, the Oxford-AstraZeneca vaccine uses the double stranded DNA.

The unique feature of the Oxford-AstraZeneca vaccine is that it uses a harmless virus as a kind of Trojan Horse to carry the genetic material of the pathogen into the cells to generate immune response. In technical parlance, the Trojan Horse is called Adenovector virus. The COVID-19 vaccine formulated by Oxford-AstraZeneca uses the common cold causing virus in Chimpanzees called ChAdOx1 as the Adenovector virus which acts as a guided missile to deliver its payload - a weakened SARS CoV-2 genetic material, into the target cells. The SARS CoV-2 virus is made impotent by genetically modifying it. It looses its ability to multiply when it enters the human body, yet it tricks the immune system to reinforce its defence.

2.2.1 The Spike Protein of SARS-CoV-2

The spike protein of corona virus causing COVID-19, forms the club-shaped protrusions that stick out all over the ball and a longer, thinner stalk, as shown in the fig.(1), resembling a crown or the sun's corona - hence the name. These spike proteins provide the key target for potential vaccines and treatments to work.

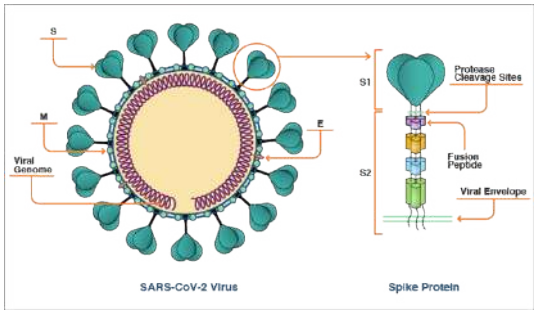

Figure 1: Viral spike protein structure
(Source: https://www.cas.org/blog/covid-19-spike-protein)

The Oxford-AstraZeneca vaccine is based on the virus's genetic instructions to building the spike protein.

2.2.2 DNA in a Protective Sheath

The Adenovector virus is first genetically modified to make it weak and impotent. The impuissant virus loses its ability to replicate thus making it a safe to be injected into human body. It can enter the cell but can not replicate itself. The DNA of the SARS-CoV-2 spike protein is encapsulated by a protective sheath made up of the Adenovirus, as shown in the fig.(2).

DNA is not as fragile as RNA molecule. Armed with the protective protein coat of the Adenovector, the DNA is robust and stable. Therefore, the Oxford vaccine doesn't have to stay

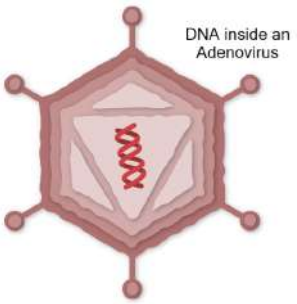

Figure 2: Viral DNA encapsulated by an Adenovirus
(Source: https://www.nytimes.com/interactive/2020/health/oxford-astrazeneca-covid-19-vaccine.html)

frozen which could potentially bring down drastically the logistic cost of handling it - a huge booster for the poor countries. In contrast, mRNA vaccines have to be kept at ultra low temperature which renders them costly and cost-ineffective.

2.3 Entering the Cell

On injecting into the upper arm, the adenoviruses bump into the human cells and latch onto the proteins on their surface. The cell engulfs the virus and drags it inside. The Adenovirus tunnels through the bubble and moves towards the nucleus of the cell where the cell's DNA is housed. Adenovirus pushes its DNA into the cell's nucleus. The impotent adenovirus can not copy itself but its payload - the spike protein of coronavirus can be read by the cell. On reading, the cell copies the spike protein code into the messenger RNA (mRNA) molecules as shown in the fig.(3).

This approach mimics what the SARS-CoV-2 does in nature – but the vaccine mRNA codes only for the critical fragment of the viral protein. This gives the immune system a preview of what the real virus looks like without causing a disease [1].

The mRNA leaves the nucleus, and the cell's molecules read its sequence and begin assembling spike proteins. Some of the spike proteins form spikes that migrate to the surface of the cell and stick out their tips. The vaccinated cells also break up some of the proteins into fragments, which they present on their surface. These protruding spikes and spike protein fragments can then be recognized by the immune system [2].

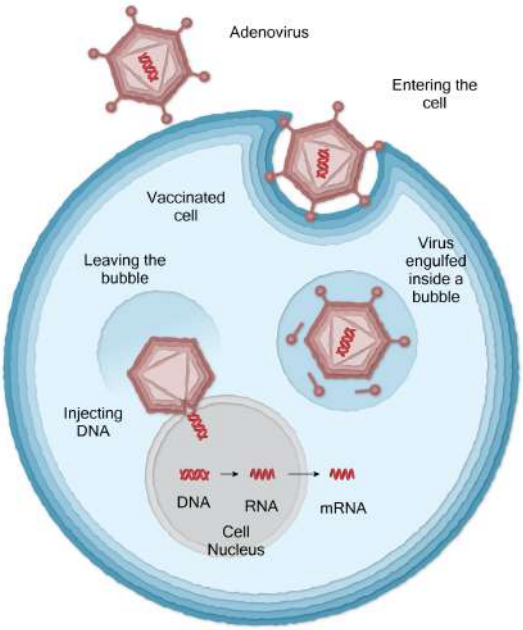

Figure 3: DNA's entry into the cell
(Source: https://www.nytimes.com/interactive/2020/health/oxford-astrazeneca-covid-19-vaccine.html)

2.4 The Triggering of the Immunity System

The protein fragments are detected by the immune cells called the antigen-presenting cells, as shown in the fig.(4). The spikes protruding out from the cell's surface are detected by the T-cells. There are two main types of T-cells: the helper T-cells and the killer T-cells. Helper T-cells stimulate the B-cells to make antibodies and help the killer cells to develop. The killer T-cells directly kill cells that have already been infected by a foreign invader. The T-cells also use cytokines as the messenger molecules to send chemical instructions to the rest of the immune system to ramp up its response.

Other immune cells, called the B-cells, may bump into the coronavirus spikes and protein fragments on the surface of vaccinated cells. A few of the B-cells may be able to lock onto the spike proteins as shown in the fig.(5). If these B-cells are then activated by helper T-cells, they will start to proliferate and pour out antibodies that target the spike protein [2].

Further reinforcement of the army of the cells to fend off the viral attack, is brought in by the killer T Cells. The antigen presenting cells activate and trigger killer T Cells which destroy the any corona-infected cells that have been turned into the virus making factories as shown in the fig.(6).

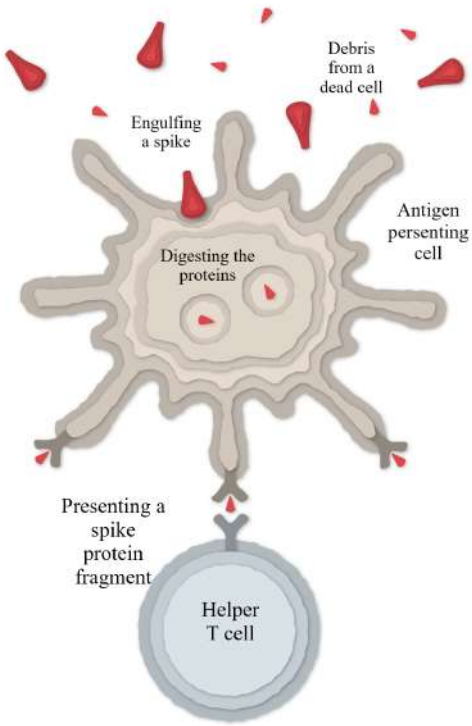

Figure 4: Antigen-presenting Cell and the T-cell
(Source: https://www.nytimes.com/interactive/2020/health/oxford-astrazeneca-covid-19-vaccine.html)

2.5 Is it Safe?

The Oxford-AstraZeneca vaccine was claimed to be 94 % effective. During the clinical trials, the vaccine was found to be highly effective at reducing cases of symptomatic illness among those who were vaccinated. It requires two jabs separated by an interval of 28 days. The second and booster dose helps the immune system to retain its memory about the viral proteins for a longer period of time. But because the vaccine is based on new technology, the researchers are wary about speaking out on the time frame for which its efficacy would last.

There are two main causes for tapering off in vaccine's efficacy. First, the antigen levels in the body decline over time and second, the strain of the virus may mutate. A mutated strain may require a new vaccine. This can go on *ad infinitum*. In the case of SARS-CoV-2, we are unsure how fast it mutates. We can, therefore, dearly hope that the virus is languid and truly reluctant to mutate so that we could tame it at the earliest.

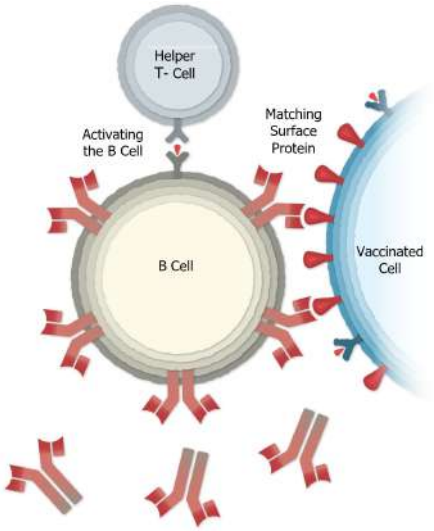

Figure 5: Activating the B Cell
(Source: https://www.nytimes.com/interactive/2020/health/oxford-astrazeneca-covid-19-vaccine.html)

2.6 Will the Vaccine Help in Reaching Herd Immunity?

A vaccine's efficacy matters when it comes to ending a pandemic. Herd immunity has been a buzzword since the pandemic began, but the misunderstanding, what herd immunity is and how it can be achieved, has been just as prevalent. Briefly, herd immunity, or community immunity, refers to having enough people in a population who are immune to a specific disease that the disease has trouble spreading much in that population. To reach herd immunity — the point at which an outbreak peters out — a vaccine must reduce the number of viral spreaders or the pool of people those spreaders can infect, or both.

The pandemic can be sustained only when an infectious person can walk into a place like a bar or a gym and find at least one new victim to infect. Eliminate the supply of potential new victims by vaccinating them all, and the virus can go nowhere [3]. Eliminate the supply of spreaders, and you may slow the pandemic even faster.

With the rapid spread of COVID-19 – and high levels of existing infection – the proportion of the world population that needs to be vaccinated is high and that is one of the biggest challenges to reach herd immunity.

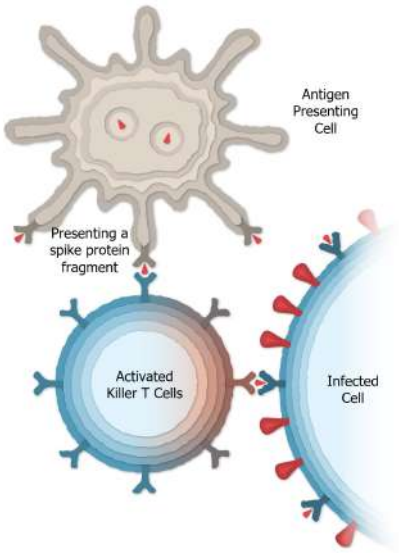

Figure 6: Killer T-cell
(Source: https://www.nytimes.com/interactive/2020/health/oxford-astrazeneca-covid-19-vaccine.html)

2.7 Challenges in the Equitable Distribution of the Vaccines

When it comes to the distribution of vaccine, we are faced with an ethical quandary: Who gets a shot first? In a damning report, Oxfam international - a global watchdog on inequality, says that nearly 70 poor countries will only be able to vaccinate one in ten people against COVID-19 next year unless an urgent action is taken by the government and the pharmaceutical industry to make sure enough doses are produced. By contrast, the wealthier nations have bought up enough doses to vaccinate their entire populations nearly three times over by the end of 2021. This flexing of muscles by the rich nation, the so called “vaccine nationalism," is a bad omen and portends a dreadful scenario in the future.

Anna Marriott, Oxfam’s health policy Manager, said: “No one should be blocked from getting a life-saving vaccine because of the country they live in or the amount of money in their pocket. But unless something changes dramatically, billions of people around the world will not receive a safe and effective vaccine for COVID-19 for years to come.”

So far, all of Moderna’s doses and 96 percent of Pfizer/BioNTech’s have been acquired by the rich countries. In contrast, Oxford/AstraZeneca has pledged to provide 64 percent of their doses to people in developing nations. Yet despite their actions to scale up the supply, they can still only reach 18 per cent of the world’s population next year at the most. The Oxford/AstraZeneca

deals have also mostly been made with some of the big developing countries like China and India, while the majority of developing countries have not done deals. These countries are in the lurch, perilously dependent on the largesse of the rich countries.

Unequal vaccine distribution is a concern that Dr. Tedros Adhanom Ghebreyesus, director of the World Health Organization, has raised repeatedly over the course of the pandemic.

“Every government rightly wants to do everything it can to protect its people," Tedros said during a November press conference. "But there is now a real risk that the poorest and most vulnerable will be trampled in the stampede for vaccines."

Unless we abandon our selfish and parochial ways, an equitable distribution of the vaccine appears a distant dream. This leaves the poorer nations at peril.

With each country putting its own interest ahead of that of humanity, it can hardly escape our attention that the complete eradication of the virus is a distant mirage and only the time will tell when it would actually materialize.

2.8 Conclusion

To vaccinate the whole world is a challenging task indeed. Even if Pfizer-BioNTech, Moderna or Oxford-AstraZeneca optimize their production, it would be nearly impossible to vaccinate half of the global population within next two years. The eradication of SARS-CoV-2 is an uphill task but not an impossible one.

The cost-effectiveness of the Oxford-AstraZeneca vaccine is likely to be a boon for the poor countries. If the poor countries use it judiciously with meticulous planning, the virus would be tamed. The Oxford-AstraZeneca vaccine would surely turn out to be the game changer which would apply brakes to the galloping virus. The scientist from the countries like China and Russia have developed their own vaccines and many others are in the advance stage of trials. To rein in the spread of the virus, each one of them will play a crucial role.

It is a make or break situation for humans and the pathogen has put our resilience to a test like never before. May the mother nature bless us with soundness of mind to overcome this protracted crisis. For the time being, I am keeping my fingers crossed!!!

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[3] Available online: https://www.latimes.com/science/story/2020-11-18/covid-19-vaccine-race-takeaways (accessed on 12 December, 2020).

3. Mutation in SARS-CoV-2: Is it a Ticking Bomb?

Dr. Pruthul Desai

The advent of vaccine has been touted as the beginning of an end of the COVID-19 pandemic. But the latest mutation of the virus in England has raised the alarm bell across the world. Questions are being raised whether the mutation will affect the efficacy of the vaccines or not. If it does, where will it leave us in this mammoth task of taming the virus. In this article, the details of the latest mutation found in England is discussed. The factors affecting the efficacy of the vaccine is also vividly discussed.

3.1 Introduction

As the curtains fall on the eventful year 2020, the COVID-19 pandemic lingers on, mutant strains of the virus and the vaccines continue to play the cat and mouse game. The latest twist in the plot is the discovery of a new variant in England. The twist in the murder mysteries by Sir Arthur Conan Doyle appear pale in comparison to the gripping story of suspense in the COVID-19 saga. No one knows exactly what is going on because the virus seems to throw surprises and challenges at regular intervals.

A new strain of the SARS-CoV-2 virus which is said to be as much as 70% more transmissible than its previous versions, has spread like wild fire in and around London sending shivers down the spine of the British Government and to a large extent caused panic across the world. Though the new strain is one of the many observed across the different parts of the world during the last eight months since the pandemic began, it could not have come at a worse time for the United Kingdom which started the mass innoculation of its subjects a two weeks back using the Pfizer-BioNTech vaccine. Whether the latest variant will be able to dodge the vaccine is the next big question which may send the entire innoculation program into tizzy spin. The same strain has also been spotted in Australia, Denmark, Italy, Iceland and the Netherlands. A similar variant found in South Africa, with some of the same mutations, is also causing concern. There are strong suspicions that both the variants may be spreading faster than expected, but this is still unclear.

The knee jerk response of the UK government and the world to this “impending crisis" was driven by panic and trepidation. Acting proactively, the UK imposed strict tier four mixing rules for the millions of people during Christmas in England, Scotland and Wales. “When the virus changes its method of attack, we must change our method of defense,” said the British Prime Minister Mr. Boris Johnson. The echoes of the actions by the UK government have

reverberated across the world and other countries have placed travel ban on the passengers to and from the UK till December 31.

For almost an entire year 2020, the SARS-CoV-2 has consumed the narrative and it relentlessly continues to do even today. Various reports, often unsubstantiated, which warn that the mutating virus may spread more rapidly, evoke visions of doomsday scenario leading to the heightened anxiety in the populace. In this undesirable scenario, a dispassionate look at the way SARS-CoV-2 has mutated and its possible implication is necessary to clear any uncertainty and ambiguity that may be pervading in the minds of millions across the globe.

3.2 What is a Mutation?

Mutation is an alteration in the genetic material (the genome) of a cell of a living organism or of a virus that is more or less permanent and that can be transmitted to the cell's or the virus's descendants. Mutations in viruses, a biological imperative, are common place and are the bedrock of the natural selection. SARS-CoV-2 virus is no exception. Nearly 4000 mutations in the SARS-CoV-2 virus have been documented since the COVID-19 outbreak. But the latest one in the UK has caused a nervous unease.

Mutations cause changes in the protein that are generated which can impact virus' ability to transmit or cause disease. While the term mutation tends to conjure up images of dangerous new viruses with the enhanced abilities sweeping across the planet, our past experience appears to suggest that the vast majority of mutations tend to have little impact on the properties of the virus and are usually inconsequential. But once in a while, the virus mutates in a manner that suddenly alters its ability to survive and reproduce. In other words, occasionally, a mutation will enable greater growth, transmissibility or escape from the immune system, in which case the mutated virus may spread widely throughout the population. It is feared that the latest mutation observed in the UK has increased the virus' ability to infect manifolds.

3.3 What Do We Know About the New Variant?

The World Health Organization (WHO) says that the coronavirus is mutating "at a much slower rate" than seasonal influenza. Scientists attribute this to the innate ability of the virus to "proof read" its replicated genome. Studies to date estimate that the novel coronavirus mutates at a rate approximately four times slower than the influenza virus, also known as the seasonal flu virus as shown in the fig.(1). Both of them are RNA viruses, yet unlike SARS-CoV-2, the influenza virus mutates much more rapidly and erratically. As a result we are forced to develop a new vaccine and take flu jabs every year to keep the virus at bay.

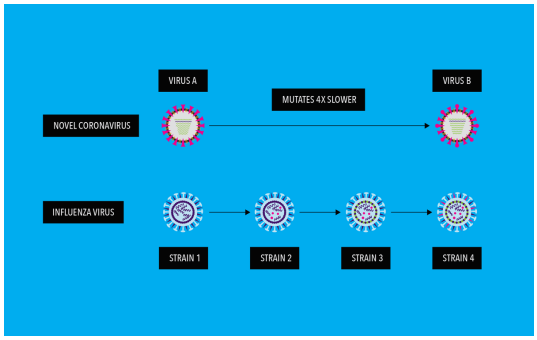

Figure 1: Schematic of the Viral Mutation
(Source: https://www.breakthroughs.com/advancing-medical-research/how-do-viruses-mutate-and-what-it-means-vaccine)

The new variant emerged as one of the most probable causes for the spike in the number of infection in London and its surrounding area. It is being referred to as VUI (Variant Under Investigation) 202012/01, or the B.1.1.7 lineage.

The variant was identified in early December in the genomic surveillance by COVID-19 Genomics UK (COG-UK), a consortium that analyses genome sequencing data from the UK. COG-UK is the largest contributor to the global Covid-19 database Global Initiative on Sharing All Influenza Data (GISAID).

The scientists have found that the variant B.1.1.17 involves 17 mutations, out of which 14 mutations cause a change in protein building blocks (amino acids) and 3 deletions (missing bits of genetic code). These mutations have altered of genes that encodes the spike protein, which the virus latch on to to enter the human cells. The vaccines made by Pfizer-BioNTech, Oxford-AstraZeneca and other companies target the spike proteins to spur immune response. If the spike protein that festoons the outside of the viral surface gets substantially changed, the efficacy of the vaccines which is particularly worrisome and worthy of serious attention, will be brought under scanner.

To unearth where the variant came from is akin to trying to find a needle in the haystack. The fact that the variant was found in the UK does not necessarily mean it originated in the UK. So, the ultimate origin of the variant B.1.1.17 will be shrouded in mystery forever. The working hypothesis of how this variant evolved is that it came from a chronically infected, immunocompromised patient who was treated with human convalescent plasma to protect against Covid-19 [1]. This gave the virus plenty of time to evolve in a way to allow it to grow despite the immune protection provided by the plasma. But, as ever, more work is required to understand if this is actually the case.

An increase in the number of infected cases apparently points towards the virus' augmented ability to infect. But the laxity in the behaviour of the public by neglecting the public health protocols could also be a significant contributor to it. Teasing apart what is due to people's behaviour and what is due to the virus is a tall order. "It remains to be seen how much of that is due to the specific genetic change in the new variant. I suspect some," said Dr. Mike Ryan, executive director of the WHO's health emergencies program. Further investigation with greater data will help us solve this mystery.

3.4 Will the Current Method of Detecting the Virus Work?

The WHO has said, "most PCR assays worldwide use multiple targets and therefore the impact of the variant on diagnostics is not anticipated to be significant." In fact, the infection triggered by the new strain in the UK, too, was detected by the conventional RT-PCR test.

It clearly means that the diagnosis of the virus will not be affected much and RT-PCR test would continue to be used as one of the most powerful diagnostic tools to detect the presence of viral infection in the body.

3.5 Will the Vaccines be Ineffective?

If the new variant is here to stay, as it appears to be, a million dollar question is: will the current vaccines be effective? The latest variant B.1.1.17 has purportedly mutated in a manner which may affect the spike protein. If the change in the form of the spike protein allows the virus a smoother and unimpeded entry into the human cells and help it evade the immune system, it could be transmitted from person to person more readily. This can have catastrophic effect on the efficacy of the vaccine.

Both the Pfizer-BioNTech and Moderna vaccines train out immune system to recognize a specific version of the spike protein. The version of the spike protein used by the vaccines was designed to match that of the old virus, not that of the B.1.1.7 virus. This means that the vaccines might become less effective than expected [2]. The question is therefore not whether the vaccines will be effective, but rather how effective they will be.

The US Centres for Disease Control (CDC) has said vaccines approved by the US Food and Drug Administration (FDA) are "polyclonal", producing antibodies that target several parts of the spike protein. "The virus would likely need to accumulate multiple mutations in the spike protein to evade immunity induced by vaccines or by natural infection," it has said.

Given the high level of efficacy of the Pfizer-BioNTech and Moderna vaccines, a reduction from the 95% we have seen so far to even 60% or 70% would still mean a very good level of

protection. The vaccine trials by AstraZeneca are underway which include a large numbers of subjects in Britain and can directly answer this question in the next few weeks.

BioNTech CEO, Ugur Sahin, recently said that its coronavirus vaccine will likely be effective against the new variant identified in Britain, but that a new version could be developed within six weeks if necessary. From a technical perspective, tweaking the vaccine co-developed with Pfizer would simply be a matter of replacing one mutation with another while the “messenger” RNA molecule remains the same.

If the efficacy of the vaccine is reduced, it becomes all the more necessary for us to get a vaccine jab and take all the precautions, so that the herd immunity is achieved at the earliest.

The WHO has said: “Laboratory studies are ongoing to determine whether these variant viruses have different biological properties or alter vaccine efficacy. There is not enough information at present to determine if this variant is associated with any change in severity of clinical disease, antibody response or vaccine efficacy.”

The effectiveness of the Pfizer vaccine or the Moderna vaccine against the mutant strains remains an ambiguous question to answer.

3.6 Conclusion

The latest variant of the coronavirus has posed a major challenge to the scientist who have worked tirelessly to produce a vaccine in record breaking time. The mRNA platform used for developing the vaccine is robust and generic. It is a matter of replacing the genome of the “older" variant with that of the “newer" variant which the scientists are confident of achieving in less than eight weeks, if need be.

The more the virus circulates, the more likely it is to mutate, making it harder to control. As an extreme case, it may render our vaccines ineffective and useless and turn our fight against the virus topsy-turvy. The latest challenge is a stark reminder that we have to tighten our belts and strictly follow the public health advisories put out by the government.

The threat posed by the new variant is ominous, but we are confident of rising up to the challenge. The road leading to the finish line of the COVID-19 saga is long and meandering with the destination being far removed as yet.

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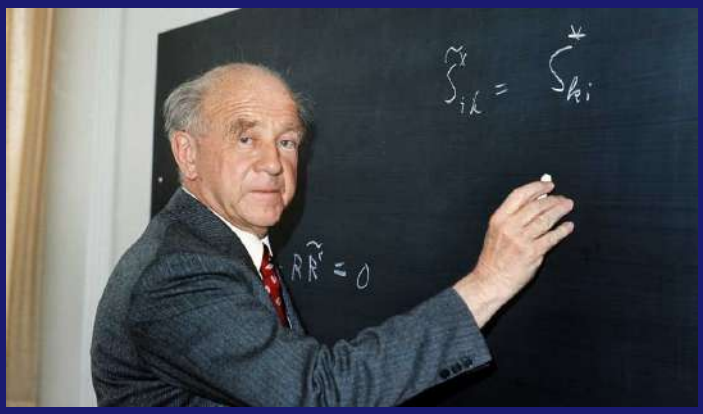
Warner Heisenberg



December 5, 1901 - February 1, 1976

Famous Quotes

- I am firmly convinced that we must never judge political movements by their aims, no matter how loudly proclaimed or how sincerely upheld, but only by the means they use to realize these aims.
- Many people will tell you that an expert is someone who knows a great deal about the subject. To this I would object that one can never know much about any subject. I would much prefer the following definition: an expert is someone who knows some of the worst mistakes that can be made in the subject, and how to avoid them.
- The existing scientific concepts cover always only a very limited part of reality, and the other part that has not yet been understood is infinite. Whenever we proceed from the known into the unknown we may hope to understand, but we may have to learn at the same time a new meaning of the word 'understanding.'
- Not only is the Universe stranger than we think, it is stranger than we can think.
- What we observe is not nature itself, but nature exposed to our method of questioning.