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EDITORIAL

VACCINE: PRAYER AND WAR

Everyone is praying now for a vaccine to end this Covid-19 pandemic. Scientists around the world are desperately trying to find a vaccine, drug or therapy to save people from the threat of this killer virus. As of August 21, 231 vaccine candidates are in the fray. Out of these only 24 candidates are supposed to be undergoing clinical trials, of which 6 are now at the beginning of phase III and 18 in phase I and II. None of the candidates has undergone a complete clinical trial so far in order to prove its efficacy. In fact, we don't even know whether any of these endeavours will ultimately succeed in producing a safe and effective vaccine. Biology is a complex subject to me, more complicated than natural sciences like physics or mathematics. This is because the immune system of humans, that resists and destroys pathogens (virus, bacteria, fungus etc.) from entering the human body, is very complex comprising several cooperative phenomena (akin to many-body problems in physics). Equally complex is the way the present virus of Covid-19 operates in the body. Conservatively speaking, the probability of success for a vaccine in the preclinical phase is only around 7%, rising to 15-20% for vaccines that reach the clinical tests. Thus, it is not a matter of surprise that most of the vaccine candidates fail to succeed.

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Everyone is under threat from the invisible enemy and each morning as we wake up, we want to make sure that we are safe and unaffected. There are basically three ways to remain unaffected by the virus. First and foremost, if we could totally avoid the entry of the virus into our body; secondly, if we could maintain our immune system strong enough to resist any attack of the virus; and lastly if attacked at all, defeat the virus by medication and other health support like supply of oxygen etc. What is most distressing to the common people is that so many people are succumbing to the attack of such a tiny pathogen, ascribing it to the inadequacy of our medical system. In order to understand the cause we need to recognize how Covid-19 virus works and how our immune (defence) system reacts to the pathogen. It is not always that death is due to the virus itself. It can very well be the reaction of our immune system under attack.

Let us start from stage 1 when the virus makes its entry into a human body. By now, we are all familiar with the photograph of a corona virus which contains lollipop-shaped "spike" proteins arranged in the form of a crown or corona which gives the name of the virus. Incidentally, the biological name of the corona virus is SARS-CoV-2, on similar lines as the

MERS and SARS, because they also contain spike proteins. When the virus enters the body, the tip of these spike proteins bind to a receptor found in some human cells and the virus then takes control of or 'hijacks' the entire machinery of human body, thereby putting normal functioning of the body go haywire. Bacteria copy themselves and proliferate while viruses do not copy themselves but use host cells for copying their viral genomes and turn them into viral proteins. It then becomes very difficult to distinguish between a normal human cell and its clone or duplicate.

Handling bacteria using antibiotics is simpler as it can distinguish between bacteria and human cells. However, it is hard to distinguish between "human and virus-hijacked human" according to immunologists. Therefore, developing antivirals is more complex and requires more precision for targeting only those human cells which have gone erratic.

The best thing therefore, would be to stop the corona virus by any means, by vaccine, drug or therapy, from hijacking the human cellular machinery. In order to do that one has to understand each of the 29 proteins, their characteristics, structure and their functioning at the molecular level. A group of scientists around the globe are doing just that to identify each protein and its structure. Another group is working to determine how these 29 proteins interact with human cells to find a drug that will target the host instead of the virus. This indirect method may help the host cells to refuse copying the viral genomes without interfering with the cell's normal functions. Hundreds of existing and experimental drugs related to SARS and MARS are also being tested for Covid-19. Use of existing drugs is being considered for Covid-19 as this is the fastest way to get some relief, particularly for mildly ill patients, thereby preventing them from becoming severely ill. Several clinics are also trying to inject antibody-rich plasma from Covid-19 survivors into patient's body.

Immunity, to common people, means ability to resist getting infected so that they become immune to infections. To an immunologist it means that the immune system has responded to a pathogen (bacteria, virus, fungus or any foreign element) when it enters the body by producing antibodies or strengthening its defence mechanism. Immune response depends on "how effective, numerous and durable those antibodies" are. Immunity is then a matter of degree and not absolute. We don't know our own tolerance from today to tomorrow. That is why some people become seriously ill than others with the same infection. This is also at the core of many such questions like will vaccination work and for how long, can infected people fall sick again from the same virus etc.

As soon as the cells sense some unknown pathogens entering the human body, they produce some proteins called cytokines. These proteins send a squad of warriors (white blood cells) to attack the virus, bombarding them with deadly chemicals and releasing more cytokines. Symptoms such as inflammation, temperature, swelling, soreness etc. are indicative that the immune system has started working. These are the actions of what's called the innate or inherent immune system. This is generic, acting in a similar way in every one, in animals too, and is marked by its speed which occurs within minutes of the virus' entry. It tries to blow out anything that seems uncommon to humans without any consideration of the specific characteristics of the pathogen. Its job is to shut down any infection as soon as possible, failing which it calls out for specialists.

Whether this nationalistic spirit is right or wrong is a different matter but it runs against the fundamental principles of vaccine development and global public health. It deprives the disadvantageous countries with limited resources from getting the vaccine for its masses.

These specialists are T-cells. They are specialized white blood cells who are selective defenders that can destroy a specific virus. Some of them act aggressively and are violent enough to blow up the infected respiratory cells in which the viruses are hiding; others are helpers which boost the immune system. These helper T-cells activate the B-cells that produce antibodies. Antibodies are small molecules which deactivate the virus so that it can no longer stick to the host cell. In a way, antibodies clear the viruses around our cells while T-cells kill those which are inside our cell. T-cells destroy the virus itself while antibodies clean up the mess. For any new virus, we should have the specific T-cells to fight that virus.Vaccines need to produce corona virus specific antibodies. These T-cells and antibodies are known as adaptive immune system which are much slower but more precise than the innate kind. Finding and activating the

right cells can take several days. It is also long lasting and has a memory of its own.

After the virus is cleaned, most of these T-cells and B-cells die down. But a small fraction of them, a veteran Covid-19 2020 warrior, remains within the blood stream. If the same virus attacks again, these "memory cells" immediately get into action and launch an adaptive branch of the immune system without the usual days-long delay. Memory is the basis of immunity as we colloquially know it—a lasting defence against whatever had made us sick in the past.

Vaccines are therefore, a mechanism to activate the immune system without falling sick. They can be made with weakened viruses, inactivated viruses, the proteins from a virus, a viral protein grafted onto a harmless virus, or even just the mRNA that encodes a viral protein. A lot remains unknown about its long term effect.

Vaccine induced immunity is believed to be weaker than the immunity gained by infection. Whether a vaccine against Covid-19 virus will give complete protection is an open question. How soon we will get the vaccine is still uncertain but we are confident that vaccine will be available sooner or later. "There was never a night or a problem that could defeat sunrise or hope".

There remain other geopolitical issues regarding availability of the vaccine in different countries. A lot will depend on which nation discovers first an effective vaccine and its relationship with others. Distribution of vaccines in a populous country like India will also be a critical issue. Another basic yet important logistical problem will be to manufacture millions of ampoules to distribute the vaccine.

In fact the 'Vaccine War' has already started. Who will get the priority of distribution of doses and whether the vaccine will reach those who need it most are the moot points of the issue now. Countries like USA, India and Russia are trying to secure priority access to the vaccine for their own citizens before they are made available to other countries. This can be possible only through pre-purchase agreements between a government and a vaccine manufacturer. The US tried to get exclusive rights of the vaccine to be developed by a German manufacturer Cure Vac which prompted the German government to comment "Germany is not for sale". Germany announced that a vaccine developed in Germany had to be made available to Germany and the whole world. Sanofi, a French Company, was forced to change its stance from "right to the largest pre-order" to the US to that it would not negotiate priority rights with any country, after public outcry and protest. In India, Serum Institute, which is in the lead for developing a vaccine, has already indicated that if the development of the vaccine succeeds, most of the initial batches of vaccine will be distributed within India.

Interestingly, India, along with the US and Russia, is reluctant to join the WHO's initiative of "Access to Covid-19 Tools Accelerator: A global collaboration to accelerate the development, production and equitable access to new Covid-19 diagnostics, therapeutics and vaccines". Whether this nationalistic spirit is right or wrong is a different matter but it runs against the fundamental principles of vaccine development and global public health. It deprives the disadvantageous countries with limited resources from getting the vaccine for the masses. ❐

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