RNA VIRUSES: "DEAD OR ALIVE"

New threat to the humanity

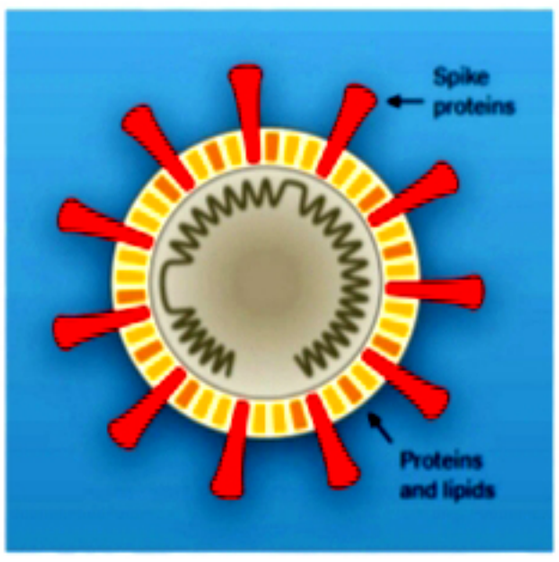
SANDEEP BARUAH

"The domestic cat would be at a loss to understand this herbivores' delight as being a paradise designed for it. This is because to the cat descended from African wild cats circa 8000 BCE in the Middle East would find it nearly impossible to believe it as true." - *Leviak B. Kelly*

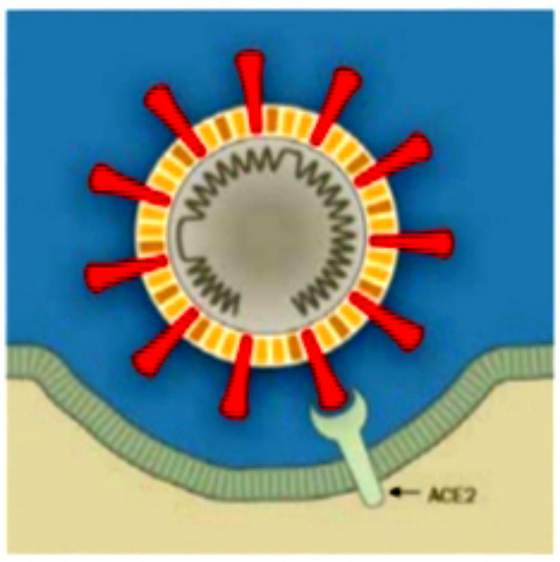
It is not only humans, but other animals and plants as well who have their own unseen enemies looming around and lurking everywhere which we call the pathogens – microscopic organisms that we don't see with our naked eyes. They are of different sizes and shapes and essentially a part of the biosphere. Though they are a part of the biosphere, they are undesirable for our existence as they cause diseases in us. There are other microorganisms which are beneficial to us. What may cause diseases in us may not to be harmful for others animals. Symbiosis and parasitism are inevitable consequences of the evolutionary biology on Earth. While symbiosis is a relationship between two types of animal or plant in which each provides for the other the conditions necessary for its existence, parasitism too is a symbiotic relationship between species, where one organism, the parasite, lives on or in another organism, the host, causing it some degree of harm. Pathogens are generally infectious biological agents that cause disease or illness to the host disrupting the normal physiology of a multicellular animal or plant.

We can draw a simple analogy here. For a rabbit, a fox may be its enemy (because the fox has to eat the rabbit for its survival) or for a deer a tiger is its enemy. So, they have an antagonistic relationship, which is paradoxical in nature as the very survival of the animal kingdom necessitates some kind of brutality. Similarly, the unseen pathogens lurking to hunt us is because they too need food for their survival and proliferation.

But are viruses living entities? We can simply describe a living entity or a life form as an organism that can grow, reproduce, respond to stimuli, and carry out various metabolic processes. The populations of living organisms also evolve over time. But the most notable characteristics of viruses are that they are incapable of carrying out metabolic processes and reproduce on their own. The viruses can replicate only within a living host cell by hijacking the genetic material of the host cell. Viruses hijack cellular machinery of the host and trick the cell into treating the virus's genetic information as its own and transcribing and/or translating it, thereby allowing the virus to replicate and proliferate and in the process damaging the hosts cells. If we compare other life forms and take a stringent view, we can say that viruses are non-living entity, but they do evolve through mutation forming different variants waiting to attack us.



Crown like spikes protruding from a SARS-CoV-2 virus enveloped in a bubble of oily lipid molecules. The lipids falls apart on contact with soap making the virus in effective for which hand washing after touching any object ensures protection from infection



After entering through the nose, mouth or eyes, the virus attaches to cells in the airway that produce a protein called ACE2.

At this very moment we are fighting a war against the RNA virus SARS-CoV-2. It has not appeared out of nothing. In fact, it is a member of a larger group of viruses known as coronaviruses that humans have been fighting for a long time. Just as we need different foods for our survival and for our proliferation, the viruses also need to do something for their survival and proliferation, and this is what they have been doing. Unlike animals and humans, viruses do not have their own metabolism and require a host cell to replicate their self and in the process damage the host cells.

Viruses contains genetic material, making it difficult to be classified as an entirely non-living entity. Some virologists therefore consider viruses as a different type of organism on the tree of life which they call 'capsid-encoding organisms'(CEOs) and the only way that the human cell can defend itself is by learning to recognise and destroy viral genes. A vaccine essentially does it and a specific vaccine can provide the cells the strength to build up immunity to fight against a specific virus.

Naturally, the question comes to our mind why unlike many other diseases caused by viruses, it is becoming increasingly difficult for the virologists to control the newly evolving viruses? What is the reason that this SARS-CoV-2 virus (the disease it is causing is termed COVID-19) is spreading so rapidly than the other viruses? Virologists have been fighting against two types of viruses, namely DNA viruses and RNA viruses.

Without going much deeper into what is DNA and RNA suffice it to say that these are the very basic building blocks

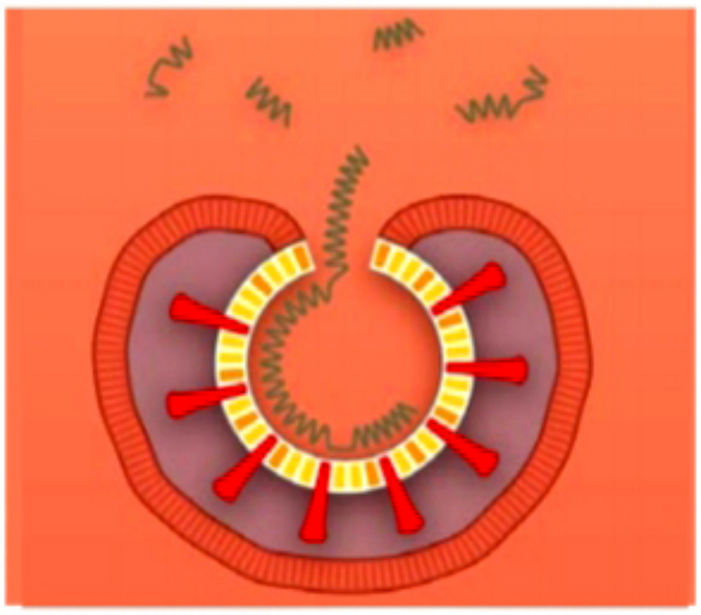
upon which life on Earth, from unicellular microscopic organisms to much complex life forms like us, are based. In the higher forms of life forms including humans, DNA is located in the mitochondria inside the nucleus of a cell while RNA is found in the cytoplasm, nucleus, and in the ribosome. DNA replicates on its own while RNA does not replicate on its own. It is synthesised from DNA when required. The function of the DNA is to transmit the genetic information while the function of the RNA is to transmit the 'genetic code' which is necessary to create the proteins needed for our survival. The synthesis of proteins takes place at the ribosomes inside the cells. The mitochondria can be called the power plants of the cell responsible for producing the energy that we need. Without mitochondria we shall be dead within seconds and without the RNA we shall be devoid of the essential proteins that we need for our survival.

Now the question arises as to why the same materials, namely DNA and RNA, which are essential for sustaining life on Earth, are also abundant in nature in the form of viruses?

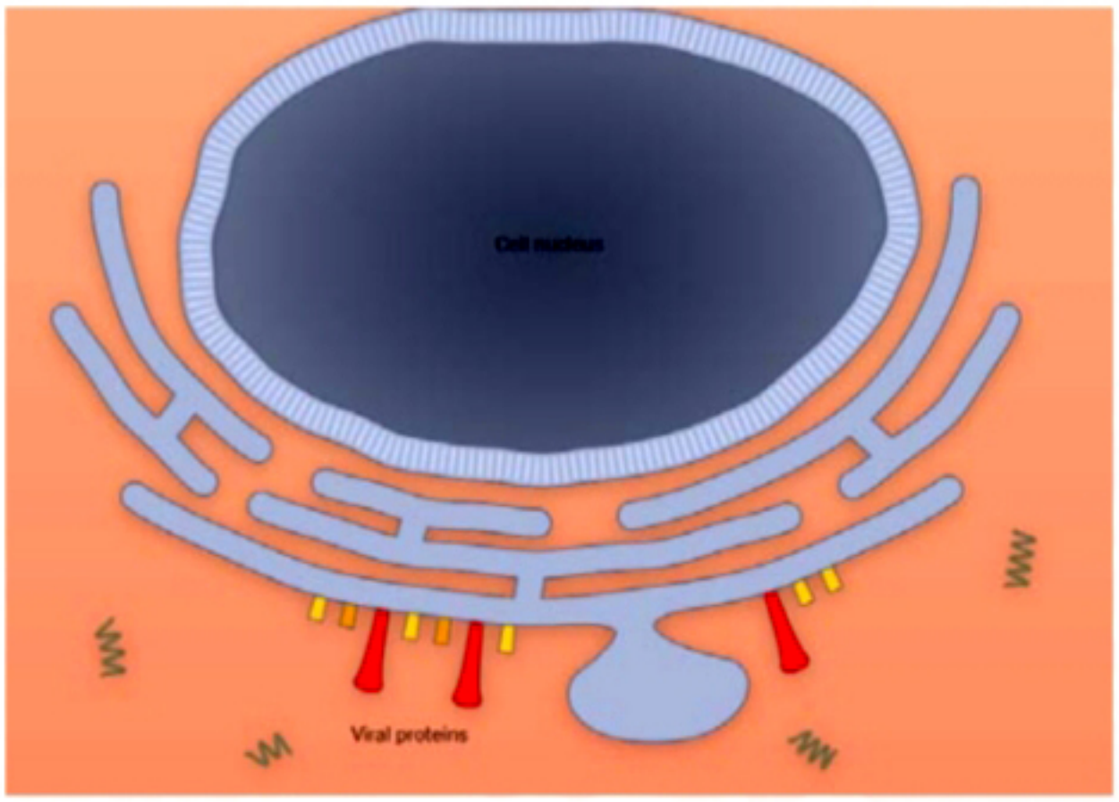
Although there are debates among virologists about how viruses appeared on Earth, there are three main hypotheses:

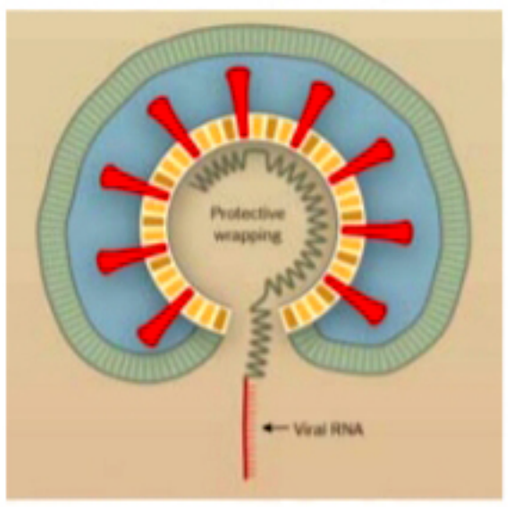
1. The progressive, or escape, hypothesis states that viruses arose from genetic elements that gained the ability to move between cells;
2. The regressive, or reduction, hypothesis asserts that viruses are remnants of cellular organisms; and
3. The virus-first hypothesis states that viruses predate or co-evolved with their current cellular hosts.

An RNA virus is a virus that has RNA (ribonucleic acid) as its genetic material. This nucleic acid is usually single-stranded RNA (ssRNA) but may also be double-stranded RNA (dsRNA). Some of the notable human diseases caused by RNA viruses include Ebola virus disease, SARS, MERS, rabies, common cold, influenza, hepatitis C, hepatitis E, West Nile fever, polio and measles, and of late COVID-19. Though there are different rabies viruses that can kill us (for example, from the bite of a dog infected with rabies virus), we now have vaccines against rabies. This has been possible because the rabies-causing virus has not mutated for a long time. So, once the vaccine is developed we can protect ourselves against rabies by injecting the vaccine. Interestingly, a vaccine contains the same virus as the one that causes the disease, but in a weakened or killed form. Once injected into our body it helps in developing antibodies to fight against the disease-causing virus by stimulating our immune system. Unlike medicines, which treat or cure diseases, vaccines protect us by making us develop immunity beforehand so that our body develops the resistance against the virus.

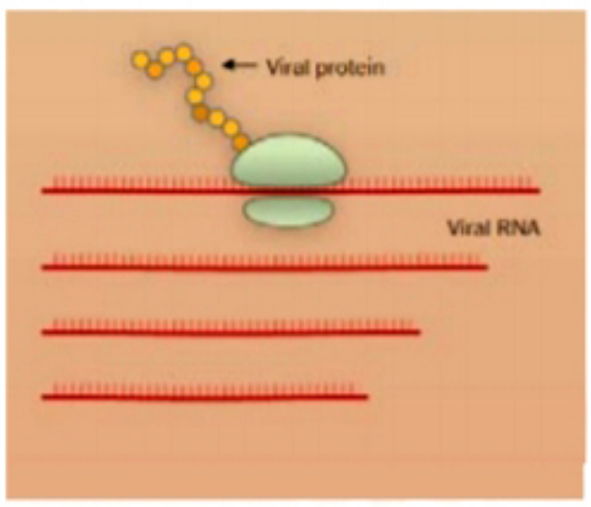


With the progress of the infection, the cell machinery starts building new spikes and other proteins allowing the formation of more copies of the coronavirus and new copies of the virus are formed





The virus infects the cell by fusing its oily membrane with the membrane of the cell. Once inside, the coronavirus releases pieces of its genetic materials called RNA in to the host cell.

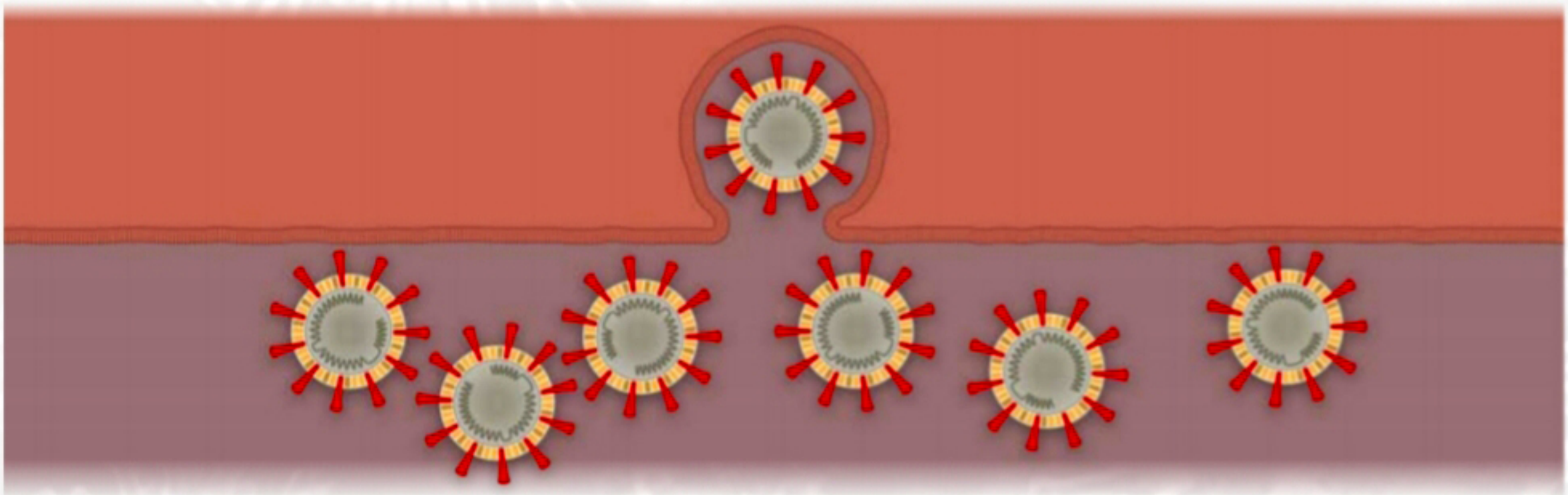


The SARS-CoV-2 virus genome is less than 30,000 genetic "letters" long. Whereas human genome is over 3 billion "letters" long. After the viral RNA enter the human cell, the infected cell reads this RNA and begins making proteins assembling new copies of the virus inside the cell. This is called the hijacking of the host cell by the virus.

Incubation period is the time elapsed between exposure to a pathogen and the time the symptoms first become apparent. In a typical infectious disease, incubation period signifies the period taken by the multiplying organism to reach a threshold necessary to produce symptoms in the host. In case of the recent outbreak, it has been found that mean incubation period of SARS-CoV-2 is in line with those of other known human coronaviruses, including SARS (mean: 5 days; range: 2 to 14 days); MERS (mean: 5 to 7 days; range: 2 to 14 days), and non-SARS human coronavirus (mean: 3 days; range: 2 to 5 days)

It has been observed that RNA viruses are more virulent than the DNA viruses due to the fact that RNA viruses can mutate fast and therefore can become more virulent and dangerous; avian influenza virus is one such virus. Hepatitis virus is a DNA virus which is less virulent than the Pox virus, which is an RNA virus.

In the recent recorded history of mankind, the biggest pandemic that wiped out 40 million people over a period of two years starting in 1918 was due to the Spanish flu virus, which is a H1N1 RNA virus. The HIV virus has killed more



Each infected cell can release millions of copies of the virus before the cell finally breaks down and dies. The viruses may infect nearby cells, or end up in droplets that escape the lungs.

than 20 million people, spread over a period of 20 years. The smallpox virus (which is a DNA virus) killed millions of people for many centuries in the past but is now extinct as a result of appropriate vaccines developed and the global immunization programme.

Of late, some of the RNA viruses are emerging as the most feared threat to our life because of their ability to kill people rapidly and to evolve very quickly. One of the reasons cited behind RNA virulence is its chemically unstable nature. While it is more prone to damage (it is said that if we wash our hand even with ordinary soap and water for 20 seconds, the outer shell/cover of the virus breaks down and the genetic material inside it becomes ineffective to cause harm), at the same time if it enters a host (human) it mutates much faster than many other viruses like the DNA viruses. RNAs are less stable than DNA and it enables them to continuously modify their genome sequence sharing a common host.

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At the time of filing this story, nearly 1,434,356 people are infected with novel coronavirus worldwide (with 82,148 deaths) within a span of last three months, making it the second largest pandemic after the 1918 Spanish flu pandemic. Virologists are at a loss to find out a cure and to understand why it is spreading so easily.

The key feature of the novel coronavirus is a protein in its surface. Some virologists are concentrating on this protein, while others are investigating to find the doorway on the human tissue known as the receptor on the cell membrane through which the novel coronavirus enters the human tissues. So, researchers have been contemplating on drugs which can target both the virus protein and cell receptor to block the entry of the virus.

The novel coronavirus (SARS-CoV-2) has 'spike proteins' which are different from its other coronavirus close relatives which bind to the human cell membrane. The process of binding to the protein site of the virus is activated by a specific cell enzyme of the host known as 'furin'. Incidentally, as furin is found in tissues of some of the vital organs of humans like the lungs, liver and small intestines, this virus can attack multiple organs. Other coronaviruses in the same genus don't have furin activation sites.

According to Gary Whittaker, a virologist at Cornell University in Ithaca, New York, USA, this furin activation site in SARS-Cov-2 "sets the virus up very differently to (other) SARS viruses in terms of its entry into cells and possibly affects stability and hence transmission." It is these activation sites (which are also found in some severe strains of influenza virus) in human tissues which is possibly enabling the virus to spread efficiently.

But according to Peter White, a virologist at the University of New South Wales in Sydney, Australia, the haemagglutinin protein on the surface of flu viruses is not similar or related to the spike protein in coronaviruses and does not have a furin activation site, but still that flu virus caused the deadliest 1918 Spanish flu.

Another group of virologists led by Prof. McLellan's in Texas has identified another feature of the SARS-CoV-2 virus. They found that the spike protein of this virus binds to a receptor on human cells known as angiotensin-converting enzyme 2 (ACE2) ten times more tightly than does the spike protein in previous SARS virus and this could probably explain why the novel coronavirus infects human cells so successfully.

Disclaimer: Contents of this article have been sourced from a number of sources (books and Internet) available with the intention of providing information on SARS-CoV-2 in the best possible way.

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