

DON'T LET IT FOOL YOU

Arun K Datta

It is very tiny. It is so tiny that you can't see it even under a microscope that you would normally use in a laboratory (Figure 1). To see it, you need a million-dollar microscope, such as, a Transmission Electron Microscope (Figure 2). It may be tiny (~ 70 nanometers), but incredibly dangerous. As of today, it has already killed more than 4.79 million people worldwide irrespective of their age, gender, economic background, race, ethnicity or religious practice. Even in the USA, which is technologically regarded as the most advanced country in the world, the death toll is more than 700,000. This monster is a virus, scientifically known as SARS-CoV-2 or **Severe Acute Respiratory Syndrome Coronavirus 2**. Under the electron microscope this virus looks



Figure 1: A Lab Microscope.

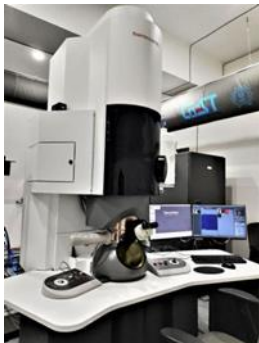


Figure 2: An Electron Microscope

like '*Coronam*', which is the Latin word for crown and, hence this name. This new virus has shown so many devastating symptoms (Front Public Health. 2020 Jul 29; 8:383) including the long-haul that has baffled most advanced scientific minds. What started as an endemic (meaning local outbreak) in Wuhan (China) in December 2019 quickly spread globally causing a pandemic (meaning global outbreak) affecting more than 200 countries. World Health Organization (WHO) coined the term Covid-19 (because it started in 2019) to distinguish this illness from other coronavirus respiratory diseases, such as, SARS (occurred in 2003). You may note that the commonly known 'flu' respiratory disease, which is caused by the Influenza virus, is unrelated to this or any other coronaviruses. Covid-19 patients were first diagnosed in USA in the beginning of 2020 (N Engl J Med, 382: 929-936, 2020). The US Government was alerted by the Chinese counterpart on January 3rd, 2020. Yet, no one could understand how dangerous this virus could be. This highly transmissible infectious disease critically affected the Public Health System creating a dire need for testing, tracing, and isolating infected individuals. It has also created a major downturn in the economy. While no death occurred from SARS (2003), this new virus for Covid-19 has already killed more than half a million people in the US alone and its carnage has not stopped yet. Its latest form, known as the delta variant, is proven more dangerous, making the public health experts more nervous.

It is true that the COVID-19 was first diagnosed in China (N Engl J Med, 382: 727-733, 2020), but where did this new coronavirus come from? This and most of the other coronaviruses is zoonotic meaning that this virus is transmitted from animals to humans. So, what is the origin of this new virus? Studying SARS (2003), scientists found that a horseshoe bat (a mammal) can serve as the natural reservoir of such viruses (Nature, 503: 535–538). This new virus, SARS-CoV-2, shares 79.6% sequence identity with SARS-CoV-1 that caused SARS (2003). Furthermore, it is 96% identical at the whole-genome level to a bat coronavirus (Nature, 579: 270-273). So, no doubt, a bat is the original source of this novel virus (Science, 310: 676–679) and, thus, this coronavirus is a mammalian virus, meaning it can infect other mammals directly. In contrast, an Influenza virus is an avian virus meaning it can't infect humans directly. Bats are nocturnal and usually live in tall trees. So, your scientific mind may ask the question: how do they come close to people for transmitting this virus? Well, there are a couple of possibilities. One possibility is that these coronavirus infected bats spread infection when virus was inhaled during handling by human (remember that

Chinese people process bat meat for marketing) and there is no coincidence that both time the initial infection occurred in China; SARS (2003) occurred in Guangdong and Covid-19 in Wuhan. Another possibility is when a carnivorous mammal, such as a civet, eats an infected bat that animal becomes infected. Those infected animals then infect humans too when they come in close contact (remember that these viruses are airborne as aerosols although they do not survive long in the air). Excretions of these bats serve as a good fertilizer. So, an alternative possibility is when the farmers handle these excretions as fertilizers, they become infected. Besides, some people suspect that Covid-19 is the result of a laboratory accident. Perhaps, during a laboratory experiment on the bats in The Wuhan Institute of Virology, SARS-CoV-2 infected the lab workers who became sick and infected other people. However, no verifiable fact is yet known for claiming this possibility. Whatever the origin of this new virus is, it has now gained the transmission capability from human to human, therefore, spreading the infection like wildfire. Anyway, the take home lesson is that this virus is very unique in infecting people with such a high transmissibility rate that everybody should be cautious, should take precautionary measures, and feel socially responsible to protect others by protecting himself/herself first. This smart choice will reduce the burden on the Public Health System, which is overwhelmed by the Covid-19 patients.

Scientists working on SARS-CoV-2 came to know that this is an RNA (ribonucleic acid) virus, meaning it can easily mutate when it gets a chance to grow (scientific term, replicate) in a human body. The Delta variant is one of such mutants. Scientists are concerned that more this virus can replicate more mutants it can create and some of those may even be more dangerous than the current delta variant (see the article at <https://www.nature.com/articles/d41586-021-02039-y> to find out how it infects us and why delta variant concerns scientists). So, the spread of this virus must be stopped. One should realize that a virus is like a particle. It can't replicate of its own. It needs a living host, such as, a human body to replicate. So, more you allow this virus to replicate within your body, chances are that it can create more mutants while trying to kill you. These newly born viruses come out from the nose as droplets of nasal mucosa of an infected person. Because these droplets remain airborne for a while, these can travel in the air to certain distance and infect others. That is the reason public health experts suggest that you should maintain a safe distance (at least 6 feet apart) from another person to be safe when you don't know if that person is carrying such virus. Better, you should also cover your nose and mouth (entry points of this virus) using face masks to be safer. By now, you might have heard of N95 masks, surgical masks, cloth masks, pleated masks, etc. N95 masks, which are regulated by the US Food and Drug Administration (FDA), are very effective in providing 95% filtration efficiency of any airborne particles including this virus. However, these single use disposable masks are costly, difficult to breathe if worn for a long time, and are usually used in a clinical set up by the healthcare workers. Surgical masks, mainly used in the surgical rooms, are also for one-time use. On the other hand, 2 to 3-layered fabric masks, which are easier to breathe in even when worn for a long time, cheaper, can be used multiple times if washed properly. The Centers for Disease Control and Prevention (CDC) recommends layered fabric masks for all others who are not healthcare workers. Also, the National Institute of Standards and Technology (NIST) showed that cotton fabric masks can partially protect an individual from getting infected (ACS Nano 2020, 14, 7, 9188–9200). Pleated fabric face masks provide better protection than non-pleated fabric face masks.

Nevertheless, such unprecedented pandemic outbreak demands the development of new preventive and therapeutic strategies besides rapidly scalable diagnostic tests to control further progress of morbidities and mortalities. Once SARS-CoV-2 was known to cause Covid-19, scientists worldwide rushed to find the cure and control this pandemic. Kudos goes to those scientists who dedicated their lives to studying this virus and understood how it infects us (and other mammals). The underlying mechanism by which this virus causes the

Covid-19 infection is different from that of Influenza virus, although the clinical symptoms are apparently similar. Earlier scientific research helped us to understand that this virus enters into the human body through the respiratory tract (via nose and mouth) and finds its 'home' in the lungs. They also came to know that the receptor-binding domain (RBD) of this virus is present in its specific protein, known as the spike protein (S; see, Figure 3), which initially attaches the host (human) protein, ACE2 or Angiotensin-converting enzyme 2 (in scientific term, spike protein is the ligand and ACE2 is the receptor in this ligand-receptor interaction). This ACE2 is present in the upper airway nasal-lining epithelial cells of the respiratory tract of the human (Cell, 182: 429-446, 2020). This ligand-receptor interaction starts a series of pathological processes that helps this virus enter into the lungs and cause a typical lesion observed by chest X-ray (Radiol Med. 2020 Jun 9: 1–8). When a patient is suspected of Covid-19 (typical clinical symptoms are fever, cough, breathing difficulties, headache, and pneumonia), detection of this virus is done by RT-PCR (reverse transcriptase - polymerase chain reaction) of the specimen from the nasal swab that can specifically identify the presence of the SARS-CoV-2 RNA (Expert Rev Mol Diagn. 2020: 1–2) by this molecular technique. The severity of this disease also lowers the oxygen level in the lungs (hypoxemia) so much that unless the patients are given supplemental oxygen from

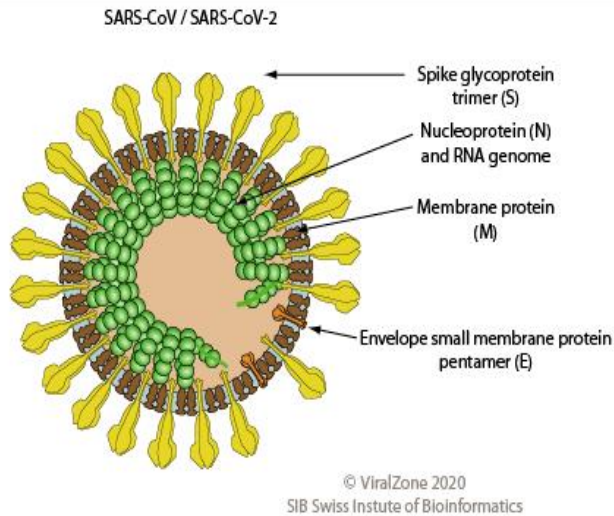


Figure 3. A schematic diagram of a Coronavirus showing the S-protein protruding from the surface. Courtesy of Swiss Institute of Bioinformatics (Lausanne, Switzerland).

an external source, they usually die. During this phase, patients with severe hypoxemia are kept in ventilators. Yet, some patients die because of the severity of the damages of multiple organs including the heart, kidney, and brain (JAMA. 2020 Aug 25; 324: 782-793). Two features that are notable for Covid-19 are asymptomatic and long-haul. Interestingly, a substantial number of individuals are immunocompetent to this virus. So, they do not show obvious clinical symptoms although they carry a high level of viral load. However, those individuals serve as Trojan-horse by infecting others. On the other hand, some patients suffer from multiple long-term complications even after recovery from this virus (showing negative test result). These are known as long-haul Covid-19 patients. Scientists are baffled to find the reason for these kinds of symptoms.

Because the spike protein is the first molecule of this virus that it uses for binding the host protein (ACE2), scientists rushed to develop vaccines utilizing the spike protein (or its mRNA) as a 'target' molecule, although some companies, such as, Bharat Biotech (India) used the inactivated virus for developing Covaxin. Our body's immune system responds to this spike protein to produce neutralizing antibodies. Thus, a vaccine protects an individual from a specific disease (scientific term, prophylaxis), in this case, Covid-19. So, a vaccine offers the best solution for controlling this pandemic and preventing death. Among the technologies that have been used for the vaccine development (Expert Rev Vaccines, 2021: 1–22), mRNA (messenger RNA) technology by both Pfizer-BioNTech and Moderna has shown to be remarkably effective with about 95% efficacy. Their efforts turned out to provide miraculous results. Not only they could develop these two vaccines within such a short time (normally takes years to develop a vaccine), but these have also proven to be highly effective in averting the disease and possible death. According to the scientists who are experts on this mRNA

technology, it is not possible for mRNA from the COVID-19 vaccines to be integrated into the human genome. Moreover, this mRNA technology has proven safe and very effective for providing protection against this Covid-19. By now, FDA has approved three vaccines in the US. As of today, while the Pfizer-BioNtech received full authorization, vaccines developed by Moderna and Janssen (of Johnson & Johnson) received Emergency Use Authorization (EUA; note - for our safety, FDA is very methodical). While Pfizer-BioNtech and Moderna vaccines need two doses of their vaccines for full protection with about 95% efficacy, Janssen vaccine developed using a different technology needs only one dose with about 66% efficacy. These vaccines given by intramuscular injection can be administered by a healthcare worker in any drug stores, such as, in CVS. All currently authorized and recommended COVID-19 vaccines are safe, effective, and reduce an individual's risk of severe illness, according to the CDC. As a therapeutic, Remdesivir (Gilead Corporation), which has received EUA by the FDA, is shown to improve the clinical conditions when a patient is hospitalized with severe COVID-19 (Drugs, 80: 1355-1363, 2020). However, getting infected and becoming hospitalized with severe clinical condition should not be anyone's choice. More therapeutic treatment regimens are in consideration including Merck's anti-viral oral pill, molnupiravir. However, please remember that 'prevention is better than cure'.

No matter what your religious practice or personal belief is, do not become a victim and allow this virus to invade your body. Once you allow it to replicate in your body, you will lose your freedom. Even if it is not your choice, this virus can force you to be admitted in a hospital. It may even kill you. The good news is, you can easily protect yourself by taking a vaccine unless your doctor suggests otherwise. This is free, now easily available, and the best preventive measure known against this virus. Recently, CDC recommended that if you are 65+ and/or immunocompromised, you should consider taking a booster dose. This booster dose will ensure full protection from this virus even if your humoral antibody level decreases over time (note: you can ask for antibody test if you are concerned). Getting vaccinated is not new to us. We got vaccinated since we were born. Most of us took triple vaccine (Diphtheria, Tetanus, and Pertussis as a combo vaccine) when we were 2 months old. These saved our lives. After you get vaccinated with any of these three FDA approved vaccines for Covid-19, chances are that your sickness will not be fatal even when you are infected. Moreover, if you suspect that you were closer to someone who is not yet vaccinated, wearing mask can further protect you and your loved ones. And finally, always get authenticated information from CDC's web site (<https://www.cdc.gov/coronavirus/2019-ncov/>) and consult your doctor if you have any questions or concerns.



Arun has been living in Carmel Del Mar since 1993. He teaches computer science in National University, San Diego. His research interest is in Biomedical Informatics.

Among his hobbies, he likes to travel and write about it. This article is the culmination of his *Coffee houser Adda* with Drs. Subhendra Chatterjee, Gautam Banerjee, Sujay Singh, and Saibal Poddar. Thanks to Dr. Ranjit Dasgupta of UW-Madison who provided valuable feedback on this article. This author takes full responsibility for any error and his personal views.