THE EVOLVEMENT OF CORONAVIRUS THROUGH DECADES FROM SARS TO COVID-19

Kumar Shubham, Sambit Kumar Roy, Apoorva Rai, Vinod Kumar Gupta

Abstract: Coronavirus, a virus that has led us to a global pandemic infecting more than 10 million people and killing more than half a million people worldwide. It has affected almost all the nations, be it a developing or developed country. Most people believe it to be a new virus but this virus was first found in the year 1965 from the nasal washing of a male child. The symptoms were typical to that of a common cold and it wasn’t thought to be highly pathogenic till the SARS outbreak in 2002-03. The virus has the largest genomic single stranded RNA among all RNA Viruses. This particular strain of virus i.e. SARS-CoV-2 which causes COVID-19 is believed to be originated in the wet markets of Wuhan, China. The following review deals with the history of Coronavirus briefly and the outbreak of SARS-CoV (Severe Acute Respiratory Syndrome) in 2002-03, MERS–CoV (Middle East Respiratory Syndrome) ten years later and finally about COVID-19 and its mode of transmission, diagnosis and treatment.

Index Terms - RNA Virus, SARS, MERS, common cold, pandemic, COVID-19

I. INTRODUCTION

Coronaviruses are the mainly a large family of RNA viruses which possesses single stranded RNA as genetic material. The name ‘CORONA’ came from the word ‘Crown’ as the virus looks like a king’s crown in electron microscopic view. The genomic RNA is largest among all the RNA viruses, almost 27 to 30kb long and polyadenylated. The genome is organized into six or seven sub genomic region and each region contains one or multiple reading frames which are separated by junction sequences that contain the signal for the transcription of multiple sub genomic mRNAs [1]. Unlike any other virus coronavirus is also dependent on living tissue for their reproduction; they mainly cause infections in human or any other mammals and birds.

1.1 Types of Coronavirus

Coronaviruses did not just pop up recently. They are a large family of RNA virus which was around us from a long time. Many of them can make people normal sneeze, coughing or normal cold symptoms. Scientists have divided coronavirus into four sub-groups and they are alpha, beta, gamma and delta. Seven types of these viruses can infect humans.

The four most common types are:-

- 229E (alpha coronavirus)
- NL63 (alpha coronavirus)
- OC43 (beta coronavirus)
- HKU1 (beta coronavirus)

The three less common types are

- MERS-CoV (a beta coronavirus that causes Middle East Respiratory Syndrome)
- SARS-CoV (a beta coronavirus that causes Severe Acute Respiratory Syndrome)
- SARS-CoV-2 (it is the novel corona virus that causes COVID-19)

II. HISTORY OF CORONAVIRUS

The first report of a human coronavirus was in 1965 when Tyrrell and Bynoe (1965) [2] isolated a virus from the nasal washings of a male child. The child had the same symptoms and signs of a common cold and the washing were found to be able to induce common colds in volunteers challenged intranasally. The virus was termed as B814 (after the number of the nasal washing). It could be cultivated in human embryo tracheal organ tissue but not in cell lines used at that time for growing other known etiologic agents of the common cold. At the same time, Hamre and Procknow (1966) were characterizing five "new" agents isolated from the respiratory tract of medical students with colds. One of these agents, strain 229E, was adapted to grow in WI-38 cells. Subsequently, Almeida and Tyrrell in the year 1967 showed that these isolates were morphologically identical to the viruses of avian bronchitis and mouse hepatitis [3]. McIntosh and
In January 2001, a 71-year-old man who had recently returned from Shen-zhen, China, a previously SARS-endemic area, presented in Hong Kong with a fever and productive cough. Although his SARS screening was negative, a novel group of coronavirus sequence was amplified by RT-PCR from his respiratory specimen with the use of primers that targeted conserved regions of the viral replicase gene [5]. This novel virus, designated HKU1, was genetically distinct from OC43, the other known human group II coronavirus. This virus could not be propagated in cell culture. Seroepidemiologic studies, based on antibodies reacting with a recombinant HKU1 nucleocapsid, suggested that human infection with HKU1 might be common. However, it is unclear whether the enzyme-linked immuno-sorbent and Western blot assays used to detect HKU1 antibody were also detecting cross-reactive antibody to OC43 or other human coronaviruses [6].

These zoonotic viruses, were not considered to be highly pathogenic to humans until the outbreak of severe acute respiratory syndrome (SARS-CoV) in 2002 and 2003 in Guangdong province, China, as the coronaviruses that circulated before that time in humans mostly caused mild infections in immuno-competent people. Ten years after SARS, another highly pathogenic coronavirus, Middle East respiratory syndrome coronavirus (MERS-CoV) emerged in Middle Eastern countries [7]. In both cases, wild animals, such as bats, were incriminated as natural host of these viruses, which have also spilled over to humans, using as main intermediate hosts, civets and camels, respectively.

III. Spreading of COVID-19

The current pandemic or COVID-19 is caused by the novel coronavirus or SARS-CoV-2. Current data shows that bats are the most possible initial source of the current 2019-novel coronavirus outbreak, that begun on December 2019 in Wuhan, China, apparently spreading from a “wet market” to multiple cities and provinces in China[8]. In addition, the virus has crossed international borders affecting now three other continents through international travelling[8]. In that market, local health authorities initially reported exposure to wild animals as well as seafood. However, intermediate hosts are still under scrutiny, deserving more detailed field studies assessing infection and seroprevalence against this COVID-19. Transmission modes also require specific studies and dedicated attention. As it has been suggested, not only it is the likelihood of common close contacts interacting with animals - a not uncommon scenario in such type of markets - but also the possibility of foodborne transmission from animal derived matter which has recently been highlighted to influence the current epidemic. The ever-increasing trend of cases suggesting the virus is being able to be transmitted by humans, produce secondary cases, and establish limited chains of transmission. This may lead in an adaptation to human hosts and their potential role as new stable reservoirs. These are some of the initial thoughts and questions deriving from the emerging COVID-19.

IV. Structure of SARS-CoV-2

SARS-CoV-2 is a spherical or pleomorphic enveloped particle containing single-stranded RNA associated with a nucleoprotein within a capsid comprised of matrix protein. The envelope bears club-shaped glycoprotein projections [10]. Coronaviruses possess the largest genomes (26.4–31.7 kb) among all known RNA viruses, with G+C contents varying from 32% to 43%. Variable numbers of small ORFs are present between the various conserved genes like ORF1ab, spike, envelope, membrane and nucleocapsid and, downstream to the nucleocapsid gene in different coronavirus lineages. The viral genome contains distinctive features, including a unique N-terminal fragment within the spike protein. Genes for the major structural proteins in all coronaviruses occur in the 5'-3' order [11]. SARS-CoV-2 possesses similarities like a typical CoV which contains at least six ORFs in its genome. Except for Gamma-coronavirus that lakes nsp1, the first ORFs (ORF1a/b), about two-thirds of the whole genome length, encode 16 nsps (nsp1-16). ORF1a and ORF1b contain a frameshift in between which produces two polypeptides and they are pp1a and pp1ab. These polypeptides are processed by virally encoded chymotrypsin-like protease (3CLpro) or main protease (Mpro) and one or two papain-like protease into 16 nsps. All the structural and accessory proteins are translated from the sgRNAs of CoVs. Four main structural proteins contain spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins are encoded by ORFs 10, 11 on the one-third of the genome near the 3'-terminus [12]. There are three or four viral proteins in the coronavirus membrane. The most abundant structural protein is the membrane (M) glycoprotein; it spans the membrane bilayer three times, leaving a short NH2-terminal domain outside the virus and a long COOH terminus (cytoplasmic domain) inside the virion. The spike protein (S) as a type I membrane glycoprotein constitutes the peplomers. In fact, the main inducer of neutralizing antibodies is S protein. Between the envelope proteins with exist a molecular interaction that probably determines the formation and composition of the coronaviral membrane. In the presence of tunica mycin coronavirus grows and produces spikeless, noninfectious virions that contain membrane glycoprotein but devoid of spike protein [13].
Figure: Structure of a SARS-CoV-2 coronavirus (14)

4.1 COMPARISON BETWEEN SARS-CoV, MERS-CoV AND SARS-CoV-2 (COVID-19)

The 5’UTR and 3’UTR are involved in inter and intramolecular interactions and are functionally important for RNA-RNA interactions and for binding of viral and cellular proteins [15]. At 5’ end, Pb1ab is the first ORF of the whole genome length encoding non-structural proteins with size of: 29844bp (7096aa), 29751bp (7073aa) and 30119bp (7078) in COVID-19, SARS-CoV; and MERS-CoV, respectively. Even with comparison of the spike protein at 30 end, among the coronaviruses specifically these three beta-coronaviruses, the difference was visualized, 1273aa, 21493aa, and 1270aa in COVID-19, SARS-CoV, and MERS-CoV, respectively. Genetically, COVID-19 was less similar to SARS-CoV (about 79%) and MERS-CoV (about 50%). The arrangement of nucleocapsid protein, envelope protein, and membrane protein among beta-coronaviruses are different [16].

V. Mode of transmission of SARS-CoV-2 which causes COVID-19

The following could be the mode of transmission of SARS-CoV-2 from one human body to another:

5.1 Respiratory Transmission

From the beginning, the Centers for Disease Control and Prevention (CDC) have said that SARS-CoV-2 is a respiratory virus, and as such, it is mainly transmitted between people through "respiratory droplets" when symptomatic people sneeze or cough. This idea, that large droplets of virus-laden mucus are the primary mode of transmission, guides the CDC's advice to maintain at least a 6-foot distance between one individual and another. The thinking is that gravity causes those large droplets (which are bigger than about .0002 inches, or 5 microns, in size) to fall to the ground within a distance of 6 feet from the infected person.

5.2 Aerosol Transmission

In order for the virus to be spread without being coughed or sneezed in large drops of mucus, it has to somehow be able to suspend in the air for long enough to infect another human. And that’s another complicating factor in figuring out transmission: People emit virus particles in a range of sizes, and some are small enough to be considered as aerosol, or fine particles that can stay suspended in the air for hours and can travel with air currents across tens of feet. A study published on March 17 in the New England Journal of Medicine found that virus particles that were aerosolized could remain viable for up to 3 hours.

5.3 Contact Transmission

There's one other route that's thought to play a role in the spread of COVID-19: contact transmission. In that situation, viral particles emitted from the respiratory tract of an infected individual land on a surface. Then, another person touches that object, and then touches their nose, mouth or eyes. The virus then sneaks into the body via the mucous membranes, infecting the second person. One study showed that SARS-CoV-2 could remain viable on surfaces such as cardboard for 24 hours and on plastic or steel for almost 3-4 days.

In one case study done by CDC in Singapore suggests that contact with contaminated surfaces can transmit the virus. In that case, a person who was infected with SARS-CoV-2, but not yet symptomatic, attended a church service. Later in the day, another person sat in the same seat, and also came down with COVID-19. Whether the virus was contracted via a contaminated surface, or potentially a lingering aerosol, however, couldn't be ascertained.
VI. Mode of infection by SARS-CoV-2 to cause COVID-19 in human body

COVID-19 (Coronavirus Disease 2019), the illness caused by the coronavirus, starts with droplets from an infected person’s cough, sneeze or breath. They could be in the air or on a surface that a person touches before touching his eyes, nose, or mouth. That gives the virus a passage to the mucous membranes inside the throat. Within 14 days, the immune system of that person may respond with early symptoms like a sore throat, fever, or a dry cough. The virus moves down to respiratory tract. That’s the airway that includes mouth, nose, throat, and lungs. The lower airways have more ACE2 receptors than the rest of respiratory tract. It attacks lung cells and alveolar cells and causes infection.

SARS-CoV-2 (COVID-19) binds to ACE2 receptors by its Spike and enters and infect cells. In order for the virus to complete entry into the cell following this initial process, the spike protein has to be primed by an enzyme called a protease. Similar to SARS-CoV, SARS-CoV-2 (COVID-19) uses a protease called TMPRSS2 to complete this process [17]. In order to attach virus receptor (spike protein) to its cellular ligand (ACE2), activation by TMPRSS2 as a protease is needed. After the virus enters the host cell and removes the genome coat, it is transcribed and then translated. Coronavirus genome replication and transcription takes place at cytoplasmic membranes and involve coordinated processes of both continuous and discontinuous RNA synthesis that are mediated by the viral replicate, a huge protein complex encoded by the 20-kb replicase gene [18]. The replicase complex is believed to be comprised of up to 16 viral subunits and a number of cellular proteins. Besides RNA dependent RNA polymerase, RNA helicase, and protease activities, which are common to RNA viruses, the coronavirus replicase was recently predicted to employ a variety of RNA processing enzymes that are not or extremely rarely found in other RNA viruses and include putative sequence-specific endoribonuclease, 3’-to-5’exoribonuclease, 2’-O-ribose methyltransferase, ADP ribose 10-phosphatase and, in a subset of group 2 coronaviruses, cyclic phosphodiesterase activities [19]. The proteins are assembled at the cell membrane and genomic RNA is incorporated as the mature particle forms by budding from the internal cell membranes. It causes the rupture of lung cells and results lung inflammation and also destroy alveolar cells which causes breathing difficulties and ultimately leads to pneumonia which is a positive sign of COVID-19. As cells rupture inside lung the blood vessels it also damages the blood vessels surrounding alveoli and accumulate debris and fluid inside lung which causes improper exchange of oxygen. Due to lack of oxygen blood carries less oxygen to various organs of human body like kidney, liver, heart and complete loss of function or organ failure may occur. At this stage COVID-19 may prove fatal to human body.

VII. SYMPTOMS OF COVID-19

Coronaviruses typically affect the respiratory system, causing symptoms such as coughing and shortness of breath. Some people, including older adults, are at risk of severe illness from these viruses. However, early symptoms of coronavirus may include coughing or shortness of breath. In some cases, it can cause severe damage to the lungs. Usually, the immune system will identify and respond to coronavirus early by sending special proteins, or antibodies, to fight the infection. The immune response to infection has side effects for the body, including fever. During an infection, white blood cells release pyrogens, a substance that causes fever.

Besides, there are other symptoms also:

- Runny nose
- Difficulty sleeping
- Head and body ache
- Sore throat
- Coughing
- Difficulties in breathing
- Sweats
- Chills
- Vomiting
- Lack of appetite
- Diarrhoea

Symptoms usually last while body’s immunity system fights against the virus. Symptoms might not show up straightaway. For example, people with COVID-19 may get symptoms 2-14 days after infection.

VIII. DIAGNOSIS OF COVID-19

It is often seen that during public screening for COVID-19, a device is pointed to the person’s forehead and then he is advised further accordingly. This device is a Non Contact Infrared Thermometer (NCIT) which measures the body temperature of a person. Every form of matter with a temperature above absolute zero (0 K) emits infrared radiation relative to its temperature. Infrared thermometers employ a lens to focus infrared light from an object onto a detector known as a thermopile. The function of the thermopile is to absorb infrared radiation and convert it to heat. The thermopile gets hotter as it absorbs more and more infrared energy. The excess heat is converted into electricity, which is transmitted to a detector which determines the temperature of the object. Since fever is one of the most common symptoms of COVID-19, this benefits the examiner whether a person is showing kg any symptoms of COVID-19 or not. It should be noted that this is just a preliminary test and not a confirmatory test for COVID-19.

COVID-19 can be diagnosed by the following ways:

8.1. CT SCAN OF THE CHEST

Chest CT scan is one of the best possible way to diagnose COVID-19 in patients. After CT scan the image is monitored for results. If image shows ground glass opacities and consolidation with or without vascular enlargement, interlobular septal thickening and air bronchogram then it is a positive result for COVID-19 [20].
8.2. RT-PCR METHOD
RT-PCR stands for Reverse Transcriptase – Polymerase Chain Reaction. It is another method which is used to diagnose COVID-19. In this process samples are first collected from patient’s nasal cavity, throat cavity or saliva and transferred to lysis buffer to prevent the denaturation of viral RNA. Then the sample is subjected to RT-PCR amplification on the presence of particular primer. If rapid amplification of viral RNA occurs then, that indicates the presence of SARS-CoV-2 in the sample and thus the person is COVID-19 positive [21].

8.3. RAPID ANTIBODY TESTING
This method is all about checking the presence of IgM and IgG antibodies in patient’s blood serum produced against the SARS-CoV-2 spike protein. Patient’s blood serum is tested to check the presence of IgM and IgG and if present then it is a positive result for COVID-19. Although, these kits are not advisable for confirming the diagnosis of COVID-19. They can be used only for surveillance purpose in India (as advised Indian Council of Medical Research) due to the reason that the results have shown wide variation in their sensitivity.

IX. TREATMENT AGAINST COVID-19

9.1. THERAPEUTIC STRATEGIES
There is no specific antiviral treatment recommended for COVID-19, and no vaccine is currently available. The treatment is symptomatic, and oxygen therapy represents the major treatment intervention for patients with severe infection. Mechanical ventilation may be necessary in cases of respiratory failure refractory to oxygen therapy, whereas hemodynamic support is essential for managing septic shock.

On January 28, 2020, the WHO released a document summarizing WHO guidelines and scientific evidence derived from the treatment of previous epidemics from human coronaviruses. This document addresses measures for recognizing and sorting patients with severe acute respiratory disease (SARS); strategies for infection prevention and control; early supportive therapy and monitoring; a guideline for laboratory diagnosis; management of respiratory failure and ARDS; management of septic shock; prevention of complications; treatments; and considerations for pregnant patients.

Among other therapeutic strategies, systemic corticosteroids for the treatment of viral pneumonia or acute respiratory distress syndrome (ARDS) are not recommended. Moreover, unselective or inappropriate administration of antibiotics should be avoided. Although no antiviral treatments have been approved, several approaches have been proposed such as Lopinavir/Ritonavir (400/100 mg every 12 hours), Chloroquine (500 mg every 12 hours), and Hydroxychloroquine (200 mg every 12 hours). Alpha-interferon (e.g., 5 million units by aerosol inhalation twice per day) is also used.

Preclinical studies suggested that Remdesivir (GS5734) — an inhibitor of RNA polymerase with in vitro activity against multiple RNA viruses, including Ebola — has been effective for both prophylaxis and therapy of human coronavirus infections [22]. This drug was positively tested in a rhesus macaque model of MERS-CoV infection [23].

9.2. PREVENTION
Preventive measures are the current strategy to limit the spread of cases. These strategies are focused on the isolation of patients and careful infection control, including appropriate measures to be adopted during the diagnosis and the provision of clinical care to an infected patient. For instance, droplet, contact, and airborne precautions should be adopted during specimen collection, and sputum induction should be avoided.

The WHO and other organizations have issued the following general recommendations:

- Avoid close contact with subjects suffering from acute respiratory infections.
- Wash hands frequently, especially after contact with infected people or their environment.
- Avoid unprotected contact with farm or wild animals.
- People with symptoms of acute airway infection should keep their distance, cover coughs or sneezes with disposable tissues or clothes and wash their hands.
- Strengthen, in particular, in emergency medicine departments, the application of strict hygiene measures for the prevention and control of infections.
- Individuals that are immuno compromised should avoid public gatherings.

The most important strategy for the populous to undertake is to frequently wash their hands and use portable hand sanitizer and avoid contact with their face and mouth after interacting with a possibly contaminated environment.

Healthcare workers caring for infected individuals should utilize contact and airborne precautions to include PPE such as N95 or FFP3 masks, eye protection, gowns, and gloves to prevent transmission of the pathogen.

Meanwhile, scientific research is growing to develop a coronavirus vaccine. There are over 110 prospective projects in works to find a workable cure for SARS-CoV-19 which spread from a wet market in Wuhan in December last year. Some have reached the clinical trial stage, others have shown a little less than favourable results. In recent days, China has announced the first animal tests, and researchers from the University of Queensland in Australia have also announced that, after completing the three-week in vitro study, they are moving on to animal testing. Furthermore, in the U.S.; the National Institute for Allergy and Infectious Diseases (NIAID) has announced that a phase 1 trial has begun for a novel coronavirus immunization in Washington state [24]. Oxford University’s adenovirus vaccine is also a promising vaccine for COVID-19.
9.3. DIFFERENT VACCINATION STRATEGIES FOR COVID-19

Like the SARS coronavirus, SARS-CoV-2 is believed to have originated from bats before infecting one or more mammal species sold in Wuhan animal markets. Both coronaviruses bind to similar ACE2 receptors found in the human lung [25], and both exhibit genomes of approximately 30 kb. SARS-CoV-2 exhibits approximately 89% nucleotide similarity to SARS-like coronaviruses (genus Beta coronavirus) found in Chinese bats [26]. On this basis, the early shaping of potential SARS-CoV-2 vaccine strategies built on those previously advanced for SARS. Researchers are trying to develop different vaccine by adopting different strategies, and they are as follows:

9.3.1. WHOLE VIRUS VACCINE

Live-attenuated or inactive whole virus vaccines represent a classic strategy for viral vaccinations. According to an industry newsletter, Johnson & Johnson is one of the few multinational companies embarking on COVID-19 vaccines similar to their Ebola vaccine platform, they are employing Janssen’s AdVac® adenoviral vector and manufacturing in their PER.C6® cell line technology. In addition, researchers at the University of Hong Kong have developed a live influenza vaccine that expresses SARS-CoV-2 proteins. Finally, Codagenix has developed a “codon deoptimization” technology to attenuate viruses and is exploring SARS-CoV-2 vaccine strategies. A major advantage of whole virus vaccines is their inherent immunogenicity and ability to stimulate toll-like receptors (TLRs) including TLR 3, TLR 7/8, and TLR 9. However, live virus vaccines often require extensive additional testing to confirm their safety. This is especially an issue for coronavirus vaccines, given the findings of increased infectivity following immunization with live or killed whole virus SARS coronavirus vaccines [27].

9.3.2. SUBUNIT VACCINE

Subunit vaccines for both SARS coronaviruses rely on eliciting an immune response against the S-spike protein to prevent its docking with the host ACE2 receptor. Already, under funding from the Coalition for Epidemic Preparedness (CEPI), the University of Queensland is synthesizing viral surface proteins, to present them more easily to the immune system. Moreover, Novavax has developed and produced immunogenic virus-like nanoparticles based on recombinant expression of the S-protein [27] while Clover Biopharmaceuticals is developing a subunit vaccine consisted of a trimerized SARS-CoV-2 S-protein using their patented Trimer-Tag® technology, although some full-length S-proteins for SARS also elicit increased infectivity and eosinophilic infiltration. Accordingly, a consortium led by Texas Children’s Hospital Center for Vaccine Development at Baylor College of Medicine (including University of Texas Medical Branch and New York Blood Center) has developed and tested a subunit vaccine comprised of only the receptor-binding domain (RBD) of the SARS-CoV S-protein [28]. When formulated on alum, the SARS-CoV RBD vaccine elicits high levels of protective immunity on the homologous virus challenge. An advantage of the RBD-based vaccine is its ability to minimize host immune potentiation. Initial findings that the SARS-CoV and SARS-CoV-2 RBDs exhibit more than 80% amino acid similarity and bind to the same ACE2 receptor offer an opportunity to develop either protein as a subunit vaccine.

9.3.3. NUCLEIC ACID VACCINE

Several major Bio-Tech companies have advanced nucleic acid vaccine platforms for COVID-19. For example, Inovio Pharmaceuticals is developing a DNA vaccine, while others, such as Modern Therapeutics and Curevac, are exploring RNA vaccine platforms. The concept of immunizing with DNA began with promising results in mice in 1993 showing protective immunity against influenza, but for decades, these findings have not translated to similar findings in humans. More recently, new modifications and formulations have improved nucleic acid performance in humans, with an expectation that this approach might eventually lead to the first licensed human nucleic acid vaccine [29].

X. CURRENT SITUATION OF COVID-19 WORLDWIDE

According to the data available from WHO (World Health Organization) situation report, there are total 10,185,374 confirmed cases and 503,862 deaths worldwide till 30th June, 2020. The American region has the highest confirmed cases (5,136,705) and deaths (247,129). The European region has 2,692,086 total confirmed cases and 197,254 deaths. The Eastern Mediterranean region has 1,058,055 total confirmed cases and 24,423 deaths. The South East Asia region has 784,931 total confirmed cases and 21,593 deaths. The Africa region has 566,840 cases and 347,839 recoveries. It is shocking to note that India has reported two lakh (200,000) cases in the last 12 days. This shows the rapid rate of spreading of infection and demands for people to be more careful.

XI. CONCLUSION

The national leaders of the world had declared countrywide lockdown both nationally and internationally to prevent the further spreading of COVID-19. This lockdown was aimed to prevent the social gathering which may help in slowdown the rapid spreading of COVID-19 through human contact. Although, this could not be the ultimate solution to prevent COVID-19 because as we all know, the lockdown can’t go on forever; it has to stop at some point of time. As the unlock phase begins, people need to be more and more vigilant. Till the time an efficient vaccine is found, the world has to learn to live with Coronavirus and adapt to the rules of social distancing.

There are some ways in which we are now better positioned than when we first faced the SARS-CoV-2 threat. Most importantly, we have more information about what we are facing. Current and future research is extremely valuable because we still face great uncertainty and there are momentous decisions to come.

XII. AUTHORS INFORMATION

Kumar Shubham and Sambit Kumar Roy : Both authors contributed equally to this review.
XIII. REFERENCES


[2] DAJ Tyrell, ML Bynoe; (1965); Cultivation of a novel type of common-cold virus in organ cultures. British medical journal 1 (5448), 1467.


