Novel Coronavirus Disease (COVID-19)*

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The present outbreak of the novel coronavirus initially called as “2019 novel coronavirus” or “2019-nCoV” by the World Health Organization (WHO), is also known as “Wuhan coronavirus” or “Wuhan pneumonia”, as it started in the Wuhan city of China in early December of 2019. This new coronavirus-associated acute respiratory deadly disease is now officially named as Corona Virus Disease-19 (COVID-19) by the WHO. From China, this epidemic has now spread to all over the world. On 11 March 2020, the WHO recognised COVID-19 as a pandemic. A pandemic refers to a disease that has spread to several countries, continents, if not worldwide. While the information available on this newly identified virus is limited and evolving, here is a quick run-down of what has been figured out so far.

Introduction

The new coronavirus pandemic, which is recently named as COVID-19 by WHO is the third documented spillover of an animal coronavirus to humans that has resulted in a major epidemic. The Coronaviridae Study Group (CSG) of the International Committee on Taxonomy of Viruses (ICTV), which is responsible for the classification and nomenclature of the family Coronaviridae, has assessed this virus as bat Severe Acute Respiratory Syndrome Corona Viruses (SARS-CoVs) and designated it as SARS-CoV-2 [1–3].

The novel coronaviruses infect the upper respiratory tract and lungs, leading to severe respiratory illness. While we are still not sure about the true lethality of this virus, it is continuously

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Keywords

Novel coronavirus, SARS-CoV-2, COVID-19, classification and taxonomy, symptoms, testing, chronology of events, treatment, social distancing.

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The COVID-19 pandemic that started in the Wuhan city of China in early December of 2019 has spread globally. This deadly respiratory disease caused by a novel coronavirus, SARS-CoV-2 is continuously claiming thousands of lives worldwide. WHO had earlier estimated the mortality rate due to COVID-19 around 2% and in March 2020, revised it to 3.4%.

claiming lives, and causing worldwide panic. Health officials are trying to contain the virus with travel restrictions and lockdowns.

1. What is a Coronavirus?

Coronaviruses are a group of a large family of viruses that cause diseases in mammals and birds. This mysterious virus has its name coronavirus because of its crown-shaped appearance (Latin word '*corona*' means crown). Also, it resembles the Sun's corona during a total solar eclipse. Coronaviruses are zoonotic, meaning they are transmitted from animals to humans. In humans, coronaviruses cause respiratory tract infections that are typically mild, such as some cases of the common cold (among other possible causes, predominantly rhinoviruses), though rarer forms such as Middle East Respiratory Syndrome (MERS), Severe Acute Respiratory Syndrome (SARS), and COVID-19 can be lethal [4].

Coronaviruses are large pleomorphic spherical particles with bulbous surface projections. The average diameter of the virus particles is around 120 nm. The diameter of the envelope is ~80 nm, and the spikes are ~20 nm long. The viral envelope consists of a lipid bilayer where the membrane (M), envelope (E), and spike (S) structural proteins are anchored. Inside the envelope, there are multiple nucleocapsid (N) proteins, which are bound to the positive-sense single-stranded RNA genome in a continuous beads-on-a-string type conformation. The lipid bilayer envelope, membrane proteins, and nucleocapsid protect the virus when it is outside the host cell.

Most coronaviruses that spread infections in the upper respiratory tract are not dangerous, but some that spread infections in the lower respiratory tract (windpipe and lungs) can be highly lethal, such as MERS and SARS. These viruses can cause severe pneumonia, especially in older people, people with heart disease, or people with weak immune systems. Facts about coronavirus, symptoms of infection, and how the virus spreads the infection are illustrated in *Figure 1*.

A notable outbreak of novel coronavirus (SARS-CoV) was reported in 2003. Several hundred cases of severe atypical pneumonia were reported in China in late 2002. Thereafter, similar cases were detected in Hong Kong, Vietnam, and Canada during February and March 2003. The World Health Organization (WHO) issued a global alert for the illness, designating it as “Severe Acute Respiratory Syndrome” (SARS). By April 2003, over 4300 SARS cases, and 250 SARS-related deaths were reported to WHO from over 25 countries around the world. Most of these

Figure 1. Facts about coronavirus.

The novel coronavirus infects the upper respiratory tract and lungs leading to severe respiratory illness. The older people or people with existing serious medical conditions, like heart diseases, or people with weak immune systems are vulnerable to severe illness with the virus. Common symptoms include fever, dry cough, and difficulty in breathing.

The virus is typically spread during close contact via respiratory droplets produced when people cough or sneeze. People may also catch COVID-19 by touching a contaminated surface and then touching their face. It is most contagious when people are symptomatic, although spread may be possible before symptoms appear.

cases occurred after exposure to SARS patients in household or healthcare units. The incubation period for the disease is usually from 2 to 7 days. Due to this virus, death from progressive respiratory failure occurs in about 3% to 10% of cases.

In May 2003, the sequence of the complete genome of SARS-CoV was determined. The genome of SARS-CoV is 29,727 nucleotides in length, has 11 open reading frames, and its genome organization is similar to that of other coronaviruses. Phylogenetic analyses and sequence comparisons showed that SARS-CoV is not closely related to any of the previously characterized coronaviruses.

2. What is Novel Coronavirus (SARS-CoVs-2)

SARS-CoVs-2 is the most recently discovered coronavirus that causes coronavirus disease COVID-19. Chinese scientists identified this new type of coronavirus, which was isolated on 7 January 2020 [5]. There is no vaccine for this new coronavirus and it is mutating [6–8]. Laboratory tests were conducted on all suspected cases identified through active case finding and retrospective reviews. Based on these investigations, other respiratory pathogens such as influenza, avian influenza, adenovirus, Severe Acute Respiratory Syndrome Corona Virus (SARS-CoV), and Middle East Respiratory Syndrome Corona Virus (MERS-CoV) were ruled out as the cause.

Each SARS-CoV-2 virion is approximately 50–200 nanometres in diameter and has a cobbled surface structure (human hair diameter is about 80,000–100,000 nanometres). Like other coronaviruses, SARS-CoV-2 has four structural proteins, known as the S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins; the N protein holds the RNA genome, and the S, E, and M proteins together create the viral envelope. The spike protein, which has been imaged at the atomic level using cryogenic electron microscopy, is the protein responsible for allowing the virus to attach to the membrane of a host cell. The electron micrograph of SARS-CoV-2 virion shows visible coronae (*Figure 2*). Illus-

Figure 2. Electron micrograph of SARS-CoV-2 virion with visible coronae. (Image source: *Wikipedia*).

tration of SARSr-CoV virion is given in *Figure 3*.

Modelling of the spike protein of the virus suggested that SARS-CoV-2 has sufficient affinity to the angiotensin-converting enzyme 2 (ACE 2) receptors of human cells to use them as a mechanism

Figure 3. Illustration of a SARS-CoV-2 virion. (Image source: *Wikipedia*).

Researchers suggest the cross-species transmission of this new coronavirus. The virus is formed from a combination of a coronavirus found in Rufous bats and another coronavirus of unknown origin.

of cell entry. Studies have shown that SARS-CoV-2 has a higher affinity to human ACE 2 than the original SARS virus strain [4].

COVID-19 is a new disease, and there is limited information regarding the risk factors for this severe disease. Based on currently available information and clinical expertise, older adults of over 60 years and people of any age who have serious underlying medical conditions (comorbidities) might be at higher risk of developing the severe disease with SARS-CoV-2, which may even lead to death. The high-risk severe illness conditions include chronic lung diseases, severe asthma, serious heart conditions, severe obesity, diabetes, renal failure or liver disease, and immunocompromised conditions like cancer treatment, bone marrow or organ transplantation, immune deficiencies, poorly controlled HIV or AIDS.

3. Classification and Taxonomy of SARS-CoV-2

Viruses are mainly classified by phenotypic characteristics, such as morphology, nucleic acid type, mode of replication, host organisms, and the type of disease they cause. The formal taxonomic classification of viruses is carried out with specific guidelines by the International Committee on Taxonomy of Viruses (ICTV) system.

The classification of RNA viruses requires the consideration of their inherent genetic variability, which often results in two or more viruses with non-identical but similar genome sequences being regarded as variants of the same virus. This immediately poses the question of how much difference to an existing group is large enough to recognize the candidate virus as a member of a new, distinct group. This question is answered in best practice by evaluating the degree of relatedness of the candidate virus to previously identified viruses infecting the same host or established monophyletic groups of viruses, often known as genotypes or clades, which may or may not include viruses of different hosts. This is formally addressed in the framework of the official classification of virus taxonomy and is overseen and coordinated by

GENERAL ARTICLE

Category	Coronaviruses	Humans
Realm	Riboviria	
Order	Nidovirales	Primates
Suborder	Cornidovirineae	
Phylum	Incertae sedis	
Family	Coronaviridae	Hominidae
Subfamily	Orthocoronavirinae	Homininae
Genus	Betacoronavirus	Homo
Subgenus	Sarbecovirus	
Species	Severe acute respiratory syndrome	<i>Homo sapiens</i> -related coronavirus
Genome ID	MN908947	
NCBI Reference Sequence	NC_045512.2(19621-20658nt)	
Genome Size	29,903 Base	
Individuum	SARS-CoVUrbani, SARS-CoVGZ-02 Bat SARS CoVRf1/2004, Civet SARS CoV SZ3/2003, SARS-CoVPC4-227, SARS-CoV-2 SARSr-CoVBtKY72, SARSr-CoVRatG13 Wuhan-Hu-1, and so on	Dmitri Inanovsky, Martinus Beijerinck, Friedrich Loeffler, Barbara McClintock, Marie Curie, Albert Einstein, Hideki Yukawa, Rosalind Franklin, and so on

the ICTV [2].

Novel coronavirus (SARS-CoV-2) is a positive-sense, single-stranded RNA coronavirus. Its genome was sequenced from a patient with pneumonia during the 2019–2020 Wuhan pneumonia outbreak. Taxonomy and most apt classification scheme for SARS-CoV-2 is given in *Table 1* [4, 9].

Table 1. Taxonomy of SARS-CoV-2 Coronavirus Severe acute respiratory syndrome-related coronavirus species: classifying as 2019-nCoV and naming it as SARS-CoV-2.

4. Symptoms and Testing

SARS-CoV-2 affects different people in different ways. In this respiratory disease, most infected people develop mild to moderate symptoms and may recover without requiring special treatment. Often the patient won't even know whether he has a SARS-CoVs-2 or other cold-causing virus infection, such as rhinovirus. In some cases, the patient may develop high fever and acute viral pneumonia (severe acute respiratory syndrome), putting the life at risk.

SARS-CoV-2 pathogen is a new virus. At the moment, there is no vaccine or perfect treatment for COVID-19 available. The patients with SARS-CoV-2 are treated symptomatically with available drugs and licensed antiviral drugs.

The Common clinical signs and symptoms reported for COVID-19 include, fever, dry cough, tiredness, and shortness of breath, which quickly exacerbates to respiratory distress in few cases (older people or people with comorbidities) [10, 11]. Complications may include pneumonia and acute respiratory distress syndrome. Some other symptoms include loss of appetite, loss of smell, muscle aches, and pains, sore throat, and very few people may report diarrhoea, nausea or a runny nose. Symptoms can range in severity from very mild to severe. In about 80% of patients, COVID-19 causes only mild symptoms. Chest radiographs showed invasive pneumonic infiltrating in both the lungs.

The time between exposure and symptoms onset is typically around five days but may range from 2 to 14 days. People with mild symptoms who are otherwise healthy should self-isolate and contact their medical provider or a COVID-19 information line for advice on testing and referral. People with fever, cough or difficulty in breathing should call their doctor and seek immediate medical attention (*Box 1*).

The virus typically spreads during close contact and via respiratory droplets produced when people cough or sneeze. A respiratory droplet is a particle consisting mostly of water that is large enough to fall to the ground rapidly after being produced, often defined as having a diameter greater than $5\ \mu\text{m}$ [12]. One may expel up to 3,000 droplets during coughing, and as many as 40,000 droplets while sneezing. Someone symptomatic and infectious

could have as many as 200 million viruses in a single droplet [13]. Respiratory droplets may be produced during breathing but the virus is not considered airborne. People may also catch COVID-19 by touching a contaminated surface and then their faces. It is most contagious when people are symptomatic, although spread may be possible before symptoms appear.

The incubation period of the SARS-CoV-2 virus has not yet been

Box 1. COVID-19 and Novel Coronavirus (SARS-CoV-2)

Symptoms

- SARS-CoV-2 affects different people in different ways. Most common symptoms are fever, dry cough, fatigue, and difficulty in breathing. Some people may experience loss of appetite, loss of smell, muscle aches, and pains, sore throat, and very few people may report diarrhoea, nausea or a runny nose. People can also be asymptomatic as it may take a few days to develop the symptoms.
- Under extreme conditions, the patient will develop severe pneumonia and bronchitis.

Spread

- The virus is transmitted from person to person through small droplets while coughing, sneezing or sometimes even by talking. These droplets land on objects and surfaces around the person, where the virus can be active for a few hours. The people can catch the virus by touching these objects or surfaces, then touching their eyes, nose or mouth.
- The virus enters the respiratory systems through nose and mouth. The host cells then burst and the other nearby cells get infected with virus.

Complications

- The virus cause swelling in the respiratory systems, which can make difficult to lungs to pass oxygen into the blood stream-leading to organ failure and death.
- Severe pneumonia can lead to swelling and flooding of the fluid into the lungs. Further complications may cause death.

Prevention/Precautions

- There is a nice quote “The virus doesn’t move, people move it. We stop moving, the virus stops moving, it becomes inviable, it’s that simple”.
- Avoid close contact with people who have symptoms or are infected.
- Keep appropriate distance (6-feet) from the people.
- Wash your hands thoroughly (at least for 20 seconds) with soap and water or use an alcohol-based hand sanitizer (sanitizer should contain above 60% alcohol).
- Keep your hands and fingers away from your eyes, nose and mouth.
- Clean and disinfect objects and surfaces.
- If you have any symptom, seek immediate medical attention.

properly ascertained, but as per WHO, its current estimate is anywhere from 2 to 14 days. Some studies showed as long as 24 days. This will be refined when more data become available. Understanding the time when infected patients may transmit the virus to others is critical for control efforts. Detailed epidemiological information from more people infected is needed to determine the infectious period of SARS-CoV-2. In particular, it has to be ascertained whether transmission can occur from asymptomatic individuals or during the incubation period.

A study of the people who succumbed to the virus revealed that they were already suffering from some underlying conditions. They were either frail, had heart diseases or cancer already, which basically means that their immune system was compromised, and their bodies could not fight the virus [14]. However, the information coming in on the virus is rapidly changing; so we cannot be completely sure [15].

Laboratory testing for SARS-CoV-2 virus includes methods that detect the presence of virus nucleic acid and those that detect host antibodies produced in response to the infection [16]. The presence of viruses in samples (direct virus test) is confirmed by RT-PCR (Reverse Transcription Polymerase Chain Reaction). This test is designed to detect the RNA of the SARS-CoV-2 virus and thus confirms only active infections. The test can be done with a nasopharyngeal swab or sputum sample. The throat swabs test is only reliable in the first week of the disease. Later on, the virus can move from the throat and multiply in the lungs. For people testing in the second week, a sample is taken from the deep airways by suction catheter or sputum can be used. Test results are generally available within a few hours to 2 days.

Detection of antibodies (serology test) in the blood samples of patients can be used both for diagnosis and population surveillance.

Detection of antibodies (serology test) in the blood samples of the patients can be used both for diagnosis and population surveillance. The antibodies are usually detectable 14 days after the onset of the infection. An accurate mortality rate of the disease and the level of herd immunity in the population can be determined from the results of this test. The high-throughput automated systems in central laboratories can test hundreds of samples within

hours.

Computed tomography scan (CT scan) of the chest is also helpful to diagnose COVID-19 in symptomatic individuals but is not recommended for routine screening [17, 18]. Typical features on CT initially include bilateral multilobar ground-glass opacities with a peripheral, asymmetric and posterior distribution. Subpleural dominance, crazy paving, and consolidation may develop as the disease progresses.

Chronology of Events of COVID-19

The SARS-CoV-2 virus is believed to be zoonotic; it is transmitted from animals to humans. The retrospective review suggests that the outbreak of deadly infectious respiratory illness likely initiated in the middle of December 2019 with exposures in one seafood market in Wuhan city of Hubei province in China. This wholesale market in Wuhan sold seafood, poultry, snakes, bats, and farm animals.

The SARS-CoV-2 is a new strain that has not been previously identified in humans. Researchers suggest cross-species transmission of this newly identified coronavirus. These viruses often originate in bats but might have travelled through another species on its way to infecting humans. The novel coronavirus appears to be a recombinant virus between the bat coronavirus and an origin unknown coronavirus. The studies suggest the homologous recombination within the viral spike glycoprotein, which recognizes a cell surface receptor. The receptor-binding protein might have allowed cross-species transmission to humans. According to the researchers, the resulting virus developed a mix or recombination of a viral protein that recognises and binds to receptors on host cells. Such recognition is key for allowing viruses to enter host cells. By conducting a detailed genetic analysis of the virus and comparing it with available genetic information on different viruses from various geographic locations and host species, the investigators concluded that the SARS-CoV-2 is formed with a combination of a coronavirus found in Rufous bats and another

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coronavirus of unknown origin. It is suspected that the pangolin or snakes might have served as an intermediate host between bats and humans [19, 20]. But the disease ecologist and president of Eco Health Alliance, Peter Daszak, says that more research is needed to pinpoint the precise path of this global outbreak [21].

While the full spectrum of clinical manifestations associated with SARS-CoV-2 infections in humans remains to be determined, the independent zoonotic transmission of SARS-CoV and SARS-CoV-2 highlights the need for studying viruses at the species level to complement research focused on individual pathogenic viruses of immediate significance. This will improve our understanding of virus-host interactions in an ever-changing environment for future preparedness.

The COVID-19 rapidly spread outside China and is continuing to escalate throughout the globe. As of April 22, 2020, more than 2.5 million people all over the world have tested positive for COVID-19 while about 177,000 have lost their lives. Over 686,000 patients are reported to have recovered [22–24]. The World Health Organization had earlier estimated the mortality rate due to COVID-19 around 2%. In March 2020, it was revised to 3.4%. There is inherent uncertainty in making these sorts of estimates during an evolving outbreak [25].

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Many countries including India have evaluated the pandemic situation and have taken the “extraordinary measures” of complete lockdown to contain the virus. Airports and other transport systems are shut down, offices are closed, large gathering of peoples are prohibited, and the sanitary and disinfection efforts are strengthened. Now, in China COVID-19 appears to be under control as only a few new cases have been reported in the last few days. China has started relaxing the lockdown and other restrictions, but the rest of the world is now facing mayhem due to SARS-CoV-2.

Do We Have a Treatment in Place?

Viral diseases can be prevented using viral vaccines, which stimulate protective immunity against the virus without causing major disease. While vaccination doesn't necessarily prevent infection, the previous "priming" of the host's immune system allows for a quick response and clearance of the virus before the disease occurs (or mild disease of shorter duration). Viral vaccines may also be used in active viral infections, boosting the ability of the immune system to control or destroy the virus. Some vaccines are in continuous development because certain viruses, such as influenza and human immunodeficiency virus (HIV), have a high mutation rate.

Another way of treating viral infections is the use of antiviral drugs. These drugs often have limited success in curing viral diseases, but in many cases, they have been used to control and reduce symptoms for a wide variety of viral diseases. For most viruses, these drugs can inhibit the virus by blocking the actions of one or more of its proteins. It is important that the targeted proteins be encoded by viral genes and that these molecules are not present in a healthy host cell. In this way, viral growth is inhibited without damaging the host. There are large numbers of antiviral drugs available to treat infections, some specific for a particular virus and others that can affect multiple viruses.

Antiviral drugs can be categorized into the inhibitors of fusion, uncoating, nucleic acid synthesis, integration, protease, and release. The interaction between the virus and the host cell membrane or receptor(s) is the first phase of the viral life cycle called fusion/entry. Fusion/entry inhibitors have been used for HIV treatment. The low pH of the endosome activates M2 proton channels following virus entry to acidify the viral interior and weaken the electrostatic interaction to allow viral uncoating. Uncoating inhibitors have been used against influenza (InfV). Following uncoating, nucleic acid synthesis is the third step of the viral life cycle, which is mediated by viral enzymes, including RNA polymerase, DNA polymerase, and reverse transcriptase. So, these

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enzymes have been considered as alternative targets in many viral infections. Inhibitors that specifically target integration have been used for viral treatment. Viral proteases also signify an appropriate target for the development of novel antiviral agents. The release of new viruses from the host cell is the final step of the virus infection cycle. Some drugs inhibit this phase by acting on the viral protein involved in this process.

SARS-CoV-2 is a new coronavirus, and at the moment, there is no vaccine for the treatment of COVID-19. Although the ultimate control of emerging viral infections requires the discovery and development of effective vaccines and/or antiviral drugs, currently the symptomatic treatment of patients with available drugs and licensed antiviral drugs are being tested against the SARS-CoV-2. The antimalarial drug ‘chloroquine’, and its derivative, ‘hydroxychloroquine’, are also candidates for COVID-19 treatments [26, 27]. According to a Chinese official the drug ‘favipiravir’, developed by Fujifilm Toyama Chemical as an influenza drug (Japanese flu), showed positive results for COVID-19 patients in trials in Wuhan and Shenzhen [28].

Researchers have found that ‘remdesivir’, an experimental broad-spectrum antiviral drug originally designed to target Ebola, is highly effective at fighting the novel coronavirus in isolated cells. This treatment is not yet approved in humans, but two clinical trials for this drug have been implemented in China. One clinical trial was recently approved by the Food and Drug Administration (FDA) in the United States. China has approved the use of the antiviral drug ‘favilavir’ to treat symptoms of COVID-19. The drug was initially developed to treat inflammation in the nose and throat [29].

A cocktail of the HIV drugs ‘lopinavir’ and ‘ritonavir’ were being tested against COVID-19 in China. Though some initial results have shown them beneficial, later it was reported as not much effective. The efficiency of HIV drugs, therefore, remains largely circumstantial and unproven [30–33]. And chloroquine in high doses can prove toxic. So, at present, we are at crossroads of any effective treatment. Further, once a drug is proved safe and

effective, getting it to millions of patients around the world will require a massive manufacturing capacity.

Passive antibody or plasma therapy is being investigated as a non-vaccine method of passive immunisation. In this process, the purified and concentrated antibodies produced by the immune systems of COVID-19 survivors are infused in the patients. Viral neutralisation is the anticipated mechanism of action by which passive antibody therapy can mediate defence against SARS-CoV-2. Other mechanisms such as antibody-dependent cellular cytotoxicity and/or phagocytosis may be possible. Other forms of passive antibody therapy, for example, using manufactured monoclonal antibodies, are in development [34, 35].

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Wuhan Institute of Virology has sequenced the newly emergent pathogen's RNA and uploaded its entire 30,000-nucleotide genetic code to the cloud in January 2020 [27, 36]. Thereafter, many others, including the National Institute of Virology, Pune has isolated the strains of the SARS-CoV-2 and sequenced the genome [37]. Several organizations began work on creating vaccines for SARS-CoV-2 based on the published genome. In China, the Chinese Center for Disease Control and Prevention is developing a vaccine against the novel coronavirus. Bharat Biotech, a Hyderabad based firm has joined hands with the University of Wisconsin-Madison, and a US company FluGen, to develop a vaccine named as CoroFlu. Elsewhere, three vaccine projects are being supported by the Coalition for Epidemic Preparedness Innovations (CEPI), including one project by the biotechnology company Moderna and another by the University of Queensland. The United States National Institutes of Health (NIH) is cooperating with Moderna to create an RNA vaccine matching a spike of the coronavirus surface and is hoping to start production by May 2020 [4].

The most promising and advanced vaccine appears to be mRNA1273, which is being developed by Moderna, a Boston company. In mid-March, Kaiser Permanente Washington Health Research Institute began a safety and dosing trial on young, healthy volunteers with different doses of the vaccine. Other efforts include

INO-4800, a vaccine being developed by Pennsylvania-based Inovio Pharmaceuticals; a vaccine based on previous work against the avian coronavirus from MIGAL Research Institute in Israel [27].

5. What Should We Do Now?

There is a need for awareness; the protocols are already well established. If an individual experiences symptoms, (s)he should immediately consult the doctor. Ignoring the symptoms can lead to complications.

Herd or group immunity is described as a situation where a sufficient proportion of the population develops an immunity to a given infection such that it slows or prevents disease spread, protecting “at-risk” individuals.

There is the concept of herd or group immunity. It is described as a situation where a sufficient proportion of the population develops an immunity to a given infection such that it slows or prevents disease spread, protecting “at-risk” individuals. Immunity can be generated through natural infection or vaccination. In vaccination, a controlled amount of the antigen(s) is administered. People who become infected naturally and recover may develop lasting immunity. There are, however, some points that need to be considered. In natural infection, the dose is unknown. This means someone may receive a very high level of exposure and may develop severe disease or complications, while others may receive very low dose and this may impair the effectiveness of a future immune response. Hence, going for the natural herd immunity is perilous.

To stay protected, we have to follow the principle of social distancing. Differences in some health protocols and safety measures are explained in *Box 2*. Maintaining good hand hygiene is also important—wash your hands regularly, and do not touch your face or mouth. Wear a mask if you have COVID-19 symptoms or looking after the suspect. There is a world-wide shortage of masks, hence masks must be used wisely. A disposable face mask can only be used once. If you are not sick, a homemade 2 to 3-layers washable cloth mask is sufficient for protection when you go out. The World Health Organization (WHO) has issued some guidelines to negate misconceptions among people regard-

ing the current outbreak of COVID-19 [38].

The mathematical modeling developed by the Indian Council of Medical Research (ICMR), suggests that if one active COVID-19 patient does not follow lockdown and social distancing, he can infect 406 people in 30 days. However, if his social exposure is reduced to 75%, then he can spread it to just 2.5 people. Home quarantine of symptomatic individuals is the most effective method to contain the spread of COVID-19 infection. Studies show that home quarantine of suspected cases will reduce the overall expected number of cases by 62%, and the peak number of cases by 89% [39]. This process is described as “flattening or bending the curve,” which generally refers to the potential success of social distancing measures to prevent the sudden influx of new cases that could overwhelm healthcare systems. Flattening the curve helps in maintaining the resources (*Figure 4*). By attending to all the patients, the healthcare system can avoid severe illnesses and reduce the casualties.

Figure 4. Flattening the COVID-19 case curve.

Currently, India has witnessed cases of COVID-19 mostly related to travel and local transmission from imported cases to their immediate contacts. Community transmission of the disease has not been documented until now. Once community transmission is documented, the above strategy will undergo changes. The prolonged lockdown has severe economic consequences. It has to be relieved in stages with precautions. When the test kits are easily available, an approach of extensive testing of the population and quickly isolating the people who are positive may be followed. This is called the red zone or selective isolation as followed in South Korea.

The first case of COVID-19 in India was reported on 30 January 2020 in Kerala. As of 22 April 2020, the country has reported about 20,000 cases of COVID-19 and 640 deaths; around 4,000 patients have recovered [40–41]. ICMR has constituted a Rapid Response Team and is posting various updates on COVID-19 testing strategy, advisory, list of laboratories and FAQs (Frequently Asked Questions) on its website [42]. A high-level technical committee of Public Health Experts for COVID-19 has been established by the Government of India to guide the prevention and control activities in the country. The committee will address the ways to contain the spread of COVID-19 in the dynamically changing scenario and will provide a reliable diagnosis strategy for COVID-19 testing in India. Dedicated helplines and websites are set up for information and tackling the COVID-19 outbreak [41].

Conclusions

As SARS-CoV-2 is a new virus, we do not know how it exactly affects the people. Therefore, at the moment, no perfect treatment is available against this pathogen. The most effective tools are public health measures such as quarantines and social distancing which we must follow strictly. At present, COVID-19 patients are treated symptomatically with available drugs and licensed antiviral drugs. The influenza drug ‘favipiravir’, inflammation antiviral

drug ‘favilavir’, broad-spectrum antiviral drug ‘remdesivir’, and antimalarial drug ‘hydroxychloroquine’ have shown positive results. A cocktail of the HIV drugs ‘lopinavir’ and ‘ritonavir’ are also found effective in some trials. Encouraging results have also been reported with passive antibody therapy. Development of many vaccines against SARS-CoV-2 are at advanced stages, and human trials have already started on some of them. Hopefully, in the coming few months, an effective treatment of COVID-19 will be available.

Box 2. Social Distancing, Quarantine, Isolation, Lockdown and Curfew

These all are the health protocols and safety measures to slow down the spread of pandemic. The slowdown of outbreak reduces the burden on the healthcare system.

Social Distancing: Social distancing is used to prevent sick people coming in close contact with healthy and high-risk population. Social distancing can include :

- Reducing the social interactions by staying at home.
- Cancelling the group gatherings.
- Closing offices and working from home. Having virtual meetings whenever possible.
- Shutting schools and studying at home through online classes etc.
- Ensuring 6-feet gap between people when going out for essential services or to buy groceries.
- Conversations in the group. Opting for a namaste instead of a handshake and hugging.

Quarantine: Quarantine is for people who are suspected for COVID-19 and they need to be kept strictly away from other people. Health advisories state that people who are suspected of coronavirus exposure should quarantine themselves for 14 days to check if symptoms are starting to show. Quarantine measures can be enforced by the government. Quarantine can include the following:

- Staying strictly at home/quarantine centres.
- Staying alone and totally separate from others wherever possible.
- Strictly keeping away from public spaces and public transport.
- Using separate utensils.
- Monitoring daily for COVID-19 symptoms.
- Washing hands regularly with soap and water. Cleaning the likely contaminated surfaces.

Contd.

Box 2. Contd.

- Getting all necessities delivered at home and not stepping out.

Isolation: Isolation is usually advised for those who have been diagnosed positively for COVID-19. It is the most extreme degree of separation. The only contact for people in this case would be medical personnel.

Isolation includes:

- Living in a separate area in a medical care.
- Wearing a face mask. Not contacting anyone physically.
- Getting all necessities delivered from others.
- Have all surroundings regularly cleaned.
- Cleaning hands with soap and water quite often.

Self-isolation is a measure that must be followed if you have returned from virus infected country/area or was in face-to-face contact with COVID-19 suspect.

Lockdown: A lockdown is usually a government enforcement to slow down the constant flow of people and thus reduce the spread of virus. During a lockdown, you are allowed to perform essential activities like going for picking up groceries and medical supplies. A lockdown can include:

- Suspension of rail, air and bus public transport.
- Shutting down public offices, mass worshipping places, restaurants, cinema halls, shopping malls, gyms, swimming pools and markets etc.
- Restrictions on vehicular movement and monitoring the movement of people to track Coronavirus spread.

Curfew: A curfew is usually referring to a directive from the government to keep people off the streets for a pre-decided period. In India, Section 144 of the Criminal Procedure Code (CrPC) of 1973, deals with such emergencies. The executive magistrate of state or territory is given the authority to implement Section 144, to control the situation. Janta curfew is the self-imposed curfew by the people and hence, it has no penal actions. A curfew can include the following:

- Strict measures from the government to ensure that all the people remain indoors.
- Complete closure of markets, cinema halls and religious, social and cultural gatherings.
- Imposing fines and arrests when the rules are violated.

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