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REVIEW ARTICLE

A Review of Coronavirus Disease-2019

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ABSTRACT

There is a new public health crisis threatening the world with the emergence and spread of 2019 novel coronavirus (2019-nCoV) or the severe acute respiratory syndrome coronavirus (SARS-CoV-2). The virus originated in bats and was transmitted to humans through yet unknown intermediary animals in Wuhan, Hubei Province, China in December 2019. There have been around 96,000 reported cases of coronavirus disease 2019. The disease is transmitted by inhalation or contact with infected droplets and the incubation period ranges from 2 to 14 day. The symptoms are usually fever, cough, sore throat, breathlessness, fatigue, and malaise, among others. The disease is mild in most people; in some (usually the elderly and those with comorbidities), it may progress to pneumonia, acute respiratory distress syndrome, and multiorgan dysfunction. Many people are asymptomatic. The case fatality rate is estimated to range from 2 to 3%. Diagnosis is by demonstration of the virus in respiratory secretions by special molecular tests. Common laboratory findings include normal/ low white cell counts with elevated C-reactive protein. The computerized tomographic chest scan is abnormal even in those with no symptoms or mild disease. Treatment is essentially supportive; role of antiviral agents is yet to be established. Prevention entails home isolation of suspected cases and those with mild illnesses and strict infection control measures at hospitals that include contact and droplet precautions. The virus spreads faster than its two ancestors the SARS-CoV and Middle East respiratory syndrome coronavirus, but has lower fatality. The global impact of this new epidemic is yet uncertain.

Keywords: Microbiology, Mode of spreading, Life cycle, Diagnosis, Prevention

INTRODUCTION

The first severe acute respiratory syndrome coronavirus (SARS-CoV) outbreaks in China (in 2003), which spreads out in 29 countries so far and infected about 9000 people with more than 10% mortality.[1] Soon after five more human coronaviruses (HCoV-229E, HCoV-HKU1, HCoV-NL63, and HCoV-OC43) are found also to be associated with a range of respiratory symptoms, including high morbidity outcomes such as pneumonia and bronchiolitis.[2] In 2012, another virus Middle East respiratory syndrome coronavirus (MERS-CoV) was isolated from a patient with pneumonia in Saudi Arabia.[3] However, very recent outbreak of a more SARS-associated coronavirus (SARS-CoV-2) which one causes coronavirus disease 2019 (COVID-19) disease, a most concerned factor, nowadays, to human health. Not only the health but also it caused a disaster in human social, economic, and many other aspects of life, being the disease is highly infectious and fatal too. (Several Review by CDC, WHO, NIH, etc.). In fact, SARS-CoV-2 is originated on December 26, 2019, at Wuhan city of China, and causes a life-threatening pneumonia, and is the most pathogenic

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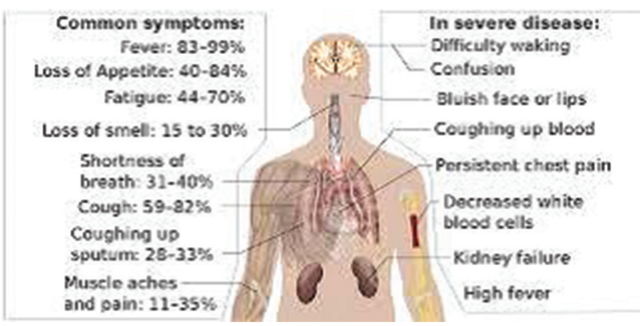
human coronavirus identified so far. No statistical data at this point would be perfect since the disease progression as well as mortality rate is increasing at an exponential rate. As of April 4, 2020, according to CNN reports, the worldwide infected cases are about 1,192,028; deaths 64,316. In the USA, infected cases are 308,533 and death 8376. In this review, we summarize the current knowledge on human coronavirus COVID-19 (since now will be mentioned a such) infection emphasizing on its impact in human life.

Coronavirus disease 2019

Another name	COVID, coronavirus
Virus strain	SARS-COV-2
Location	India
Arrival date	March 21, 2020, 1 year 1 month
Confirmed cases	25,772,440
Active cases	3,129,878
Recovered	22,355,878
Death	287,122
Specialty	Infection disease
Usual onset	2–14 days
Duration	5 days
Disease	COVID-19

SIGNS AND SYMPTOMS



Symptoms of COVID-19 are variable, ranging from mild symptoms to serve illness. Common symptoms include headache, loss of smell and test, nasal congestion and runny nose, cough, muscle pain, sore throat, fever, diarrhea, and breathing difficulties. People with the same infection may have different symptoms, and their symptoms may change overtime. Three common clusters of symptoms have been identified one respiratory symptoms cluster with cough, sputum, shortness of breath, and fever a musculoskeletal symptoms cluster with muscle joint pain, headache, and fatigue a cluster of digestive symptoms and abdominal pain, vomiting, and diarrhea. In people without prior ear, nose, and throat disorder, loss of taste combined with loss of smell is associated with COVID-19.

Of people who show symptoms, 81% develop only mild to moderate symptoms (up to mild pneumonia), while 14% develop severe symptoms and 81% develop only mild to moderate symptoms (up to mild pneumonia), while 14% develop severe symptoms (dyspnea, hypoxia, or more than 50% lung involvement on imaging) and 5% of patients suffer critical symptoms (respiratory failure, shock, or multiorgan dysfunction).

At least a third of the people who are infected with the virus do not develop noticeable symptoms at any point in time. These asymptomatic carriers tend not to get tested and can spread the disease other infected people will develop symptoms later, called "pre-symptomatic," or have very mild symptoms and can also spread the virus.

As is common with infection, there is a delay between the moment a person first becomes infected and the appearance of the first symptoms. The median delay for COVID-19 is 4–5 days. Most symptomatic people experience symptoms within 2–7 days after exposure and almost all will experience at least one symptom within 12 days. Most people recover from the acute phase of the disease. However, some people continue to experience a range of effect for month after recovery named long COVID and damage to organ has been observed.

EPIDEMIOLOGY

The outbreak was declared as "a public health emergency of international concern" by the WHO on January 30, 2020, and as a pandemic on March 11, 2020. As of April 28, 2020, there are >29 lakh confirmed cases worldwide with >2 lakh confirmed deaths. The United States have the highest number of confirmed cases. The first case of COVID-19 in India was reported on January 30, 2020, with origin from China. As of April 29, 2020, there are 22,629 active cases in India with 1007 deaths.[4] Keeping in mind the increasing number of COVID-19 cases in India, India observed a "Janata Curfew" on March 22, 2020, as insisted by our honorable Prime Minister

Narendra Modi. Later, the PM of India announced a nationwide lockdown for 21 days on March 24, 2020, so as to break the chain of transmission and the lockdown was then extended till May 3.

MICROBIOLOGY

Coronavirus is spherical or pleomorphic, single-stranded, enveloped RNA, and covered with club-shaped glycoprotein. Coronaviruses are four subtypes such as alpha, beta, gamma, and delta coronavirus. Each of subtype coronaviruses has many serotypes. Some of them were affect human of other affected animals such as pigs, birds, cats, mice, and dogs.

MODE OF SPREADING

Peoples can get the infection through close contact with a person who has symptoms from the virus includes cough hand sneezing. In general, coronavirus was spread through airborne zoonotic droplets. Virus was replicated ciliated epithelium that caused cellular damage and infection at infection site. According to a study published in 2019, angiotensin-converting enzyme 2 (ACE2), a membrane exopeptidase in the receptor used by coronavirus in entry to human cells.

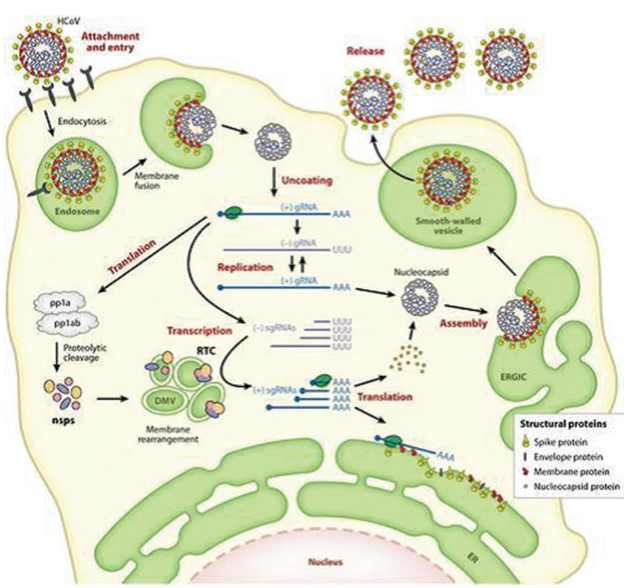
COV-2019 CONFIRMED CASES REPORT (DATE AND COUNTRY WISE) SPREADING HISTORY OF NOVEL CORONAVIRUS (2019-nCOV)

On December 31, 2019, China, East Asia, most populated country in world was informed to the WHO regarding pneumonia cases with unknown etiology. Till January 3, 2020, a total of 44 pneumonia cases were detected. On January 7, 2020, Chinese research authorities were announced that they were isolated new virus from sea food market in Wuhan city; named as 2019-nCoV. On January 13, 2020, Ministry of Public Health, Thailand, was reported one patient imported from Wuhan,
China. On January 15, 2020, the Ministry of Health, Labour and Welfare, Japan, was reported first case imported from Wuhan, China. On January 20, 2020, National IHR Focal point from the Korea was reported first case 2019-nCoV in Korea. On January 23, 2020, the United States of America was confirmed first case of 2019-nCoV in the America. On January 24, 2020, Vietnam has reported first case of 2019-nCoV with not travel history from China, while his family member was the China traveler. Hence, it's the first incidence of human-to-human transmission of coronavirus. On January 24, 2020, the Government of Singapore was confirmed first case of 2019-nCoV. On January 25, 2020, the Government of Australia, Federal Democratic Republic of Nepal and French republic were confirmed first of 2019-nCoV. Other countries also were detected and reported the cases of 2019-nCoV as on January 26, 2020 (Malaysia), January 27, 2020 (Canada), January 28, 2020 (Cambodia, Germany, and Sri Lanka), January 29, 2020 (United Arab Emirates), January 30, 2020 (the Philippines, India, and Finland), January 31, 2020 (Italy), February 1, 2020 (Russian Federation, Spain, Sweden, and the United Kingdom), February 5, 2020 (Belgium), February 6, 2020 (Japan), and February 15, 2020 (Egypt).

LIFE CYCLE OF CORONAVIRUS

Steps

1. Attachment and entry
2. Replicase protein expression
3. Replication and transcription
4. Assembly and release.



DIAGNOSIS

COVID-19 can provisionally be diagnosed on the basis of symptoms and confirmed using reverse transcription polymerase chain reaction (RT-PCR) or other nucleic acid testing of infected secretion. Along with laboratory testing, chest CT scan may be helpful to diagnose COVID-19 in individual with a high clinical suspicion of infection. Detection of a past infection is possible with serological tests, which detect antibodies to produce by the body in response to the infection.

COVID-19 VIRALTESTING

There are various methods available for COVID-19 testing, and the decision to carry out a test on suspected individuals should be made based on clinical symptoms and epidemiological factors. It would be beneficial if dental practices were provided with fast COVID-19 detection kits to test the high-risk and suspicious patients. This way, they can take necessary precautions in reducing the spread of the virus and also help the national health-care system to track the possible infected cases and gather data regarding the number of infected cases in the country. Symptoms of respiratory illness such as coughing and sneezing.

RT-PCR

As per the WHO guideline, the RT-PCR test should be done in asymptomatic or mildly symptomatic patients and those who have had contact with COVID-19-positive cases. Screening protocols and local guidelines for the patient evaluation should be followed and complied with. A crucial step in management of outbreak is fast collection of samples and testing of the suspicious cases utilizing nucleic acid amplification test (NAAT) like RT-PCR. The RNA test for the detection of SARD-CoV-2 genetic signature is used in this method. A swab is normally utilized to gather specimen from inside the nose or posterior part of throat. The result of nucleic acid testing through PCR, which is capable of detecting even a small amount of RNA, can be communicated within hours. The test is highly sensitive and specific, but its accuracy depends on the quality of the samples provided. The limitation of PCR testing is that it can only identify patients with ongoing infection, and those in the recovery phase may not have detectable virus, hence, the test could be negative. For the purpose of PCR testing, specimens should be collected from upper respiratory tract using nasopharyngeal and oropharyngeal swabs. In lower respiratory tract, specimen should be collected from the sputum (if present) or endotracheal aspirate or bronchoalveolar lavage in severely symptomatic patients. Having detected COVID-19 virus in the blood and stools of infected patients, blood and stool collected from suspicious cases can also be used for testing. The duration and frequency of shedding of COVID-19 virus in stool and potentially in urine is unknown. In deceased patients, autopsy material from lung tissue would be a useful specimen, and in recovering patients, paired serum can be used to define cases as serological assays appear.

Collection, handling, and packaging of specimens for virus detection are vital, and specimens must be delivered to the laboratory as soon as possible. If the specimen can be delivered quickly to the nominated laboratory, they can be stored and shipped at 2–8°C. In the case of delay, the use of viral transport medium is necessary, and specimen should be frozen at −20°C or ideally −70°C. It should be noted that repeated freezing must be avoided.

Serological or antibody testing

Another method of investigation in an ongoing pandemic is serological survey of cases with negative NAAT assays but strong epidemiological link to COVID-19. In these cases, paired serum samples could support the diagnosis once validated serology tests are available. The challenge of this test could be the cross reactivity with other coronaviruses. This method tests whether a suspected individual has been infected by COVID-19 and has produced antibodies. The Immunological Dent. J. 2020, 8, 53 7 of 18 reactions to the SARS-CoV-2 can take several weeks to happen, and some studies show that antibodies to COVID-19 may take 14 days to appear. Therefore, a serology test before this period may result in an unhelpful negative. Antibody test requires a blood sample from the patient, and it will look for the evidence of the virus in the body by detecting antibodies produced by the immune system in reaction to the infection. Body's first reaction to an infection is in the form of IgM as it appears in the blood approximately within 5–10 days post-infection and reaches its peak at day 21 of the infection. The time frame is vital, because if a suspicious patient develops COVID-19 symptoms, it takes about a week for their body to produce anti-COVID-19 IgM. Although for the 2019-nCoV, there is evidence of IgM presence in the blood within a day of developing symptoms, it will not be completely reliable as large quantities of IgM are not available for detection. The PCR test is reported to have a 66.7% detection rate within the 1st week of infection whereas antibody test has 38.3% detection rate. Therefore, the most reliable test for an early infection would be combination of antibody and PCR swab from suspicious patients. The combining of the tests will result in 98.6% detection rate within the first 5.5 days post-infection. Another type of antibody is IgG, which proves that a person has had the viral infection, and the body is now immune to the pathogen. This test also needs blood sample from patients, and IgG can be detected in the blood approximately 14 days after infection. If the patient becomes reexposed to the virus, the IgG level is rapidly raised within 48 h to fight the virus and prevent a new infection. Therefore, if the serology test of a patient only detects IgM, it indicates that they are within the 1st week of infection. The presence of both IgM and IgG suggests that patient should be in their 1st month of infection and theoretically immune to the virus and reinfection. IgA is another parameter that can be measured to aid the detection of infected COVID-19 cases. It is present in serum, nasal mucus, saliva, breast milk, and intestinal fluid, and it consists of around 10–15 percent of human immunoglobins. Gou *et al*. examined the humoral response of the host immune system including IgA, IgM, and IgG responses by testing 208 plasma samples from 82 confirmed and 58 probable cases (qPCR negative but with clinical symptoms) utilizing an ELISA-based assay. The median duration of IgM and IgA detection was 5 days while IgG was detected on 14 days of clinical manifestation of symptoms with a positive rate of 85.4%, 92.7%, and 77.9%, respectively. The findings suggested that the positive rates for IgM were 75.6% and 93.1% in confirmed and probable cases, respectively. It concluded that the detection efficiency of IgM ELISA method was higher than that of qPCR after 5.5 days of the symptoms' onset. The combination of IgM ELISA assay and PCR test significantly increased the positive detection rate to 98.6% for each patient. This number is 51.9% with a single PCR test. Thus, it can be concluded that the immune response of the host body can be utilized to increase the detection rate and diagnosis of COVID-19 cases.

Medical imaging

The review of the relevant literature in medical imaging suggests that chest radiographs have no diagnostic value in early stages of the infection. However, CT scan may present some findings even before the onset of symptoms. Bilateral multilobar ground-glass specificities associated with a peripheral asymmetric and posterior distribution is the typical feature of the CT in COVID-19-positive cases. As the infection develops subpleural dominance, crazy paving and consolidation can be observed in most cases. A comparative study conducted in Wuhan, the origin of COVID-19, suggests that CT is significantly more sensitive than PCR test; however, it is less specific as many of its imaging characteristics overlap with other types of pneumonia. The American College of Radiology also recommends that CT imaging should not be used as a first-line test to screen potential COVID-19 cases. The Centre for Disease Control in the U.S. recommendation is to utilize PCR testing for initial screening of suspected cases. In the UK, the Royal College of Radiologists announced that the use of additional chest CT to assess patients for the presence of likely COVID-19 infection may have a role in stratifying risk in patients presenting with acute symptoms and requiring a CT of abdomen, particularly those needing emergency surgery. In the absence of rapid access to other forms of COVID-19 testing, this is appropriate if it will change the management of the patient. However, a negative scan would not exclude COVID-19 infection, and as with all other current advice, this may change in the future.

PATHOPHYSIOLOGY

COVID-19 can affect the upper respiratory tract (sinuses, nose, and throat) and the lower respiratory tract (windpipe and lungs). The lungs are the organs most affected by COVID-19 because the virus accesses host cells through the receptor for the enzyme ACE2, which is most abundant on the surface of type II alveolar cells of the lungs. The virus uses a special surface glycoprotein called a "spike" (peplomer) to connect to the ACE2 receptor and enter the host cell. Whether SARS-CoV-2 is able to invade the nervous system remains unknown, however it is clear that many people with COVID-19 exhibit neurological or mental health issues. The virus is not detected in the CNS of the majority of COVID-19 people with neurological issues. However, SARS-CoV-2 has been detected at low levels in the brains of those who have died from COVID-19, but these results need to be confirmed loss of smell results from infection of the support cells of the olfactory epithelium, with subsequent damage to the olfactory neurons. SARS-CoV-2 could cause respiratory failure through affecting the brain stem as other coronaviruses have been found to invade the CNS. While virus has been detected in cerebrospinal fluid of autopsies, the exact mechanism by which it invades the CNS remains unclear and may first involve invasion of peripheral nerves given the low levels of ACE2 in the brain. The virus may also enter the bloodstream from the lungs and cross the blood–brain barrier to gain access to the CNS, possibly within an infected white blood cell. Tropism and multiple organ injuries in SARS-CoV-2 infection. The virus also affects gastrointestinal organs as ACE2 is abundantly expressed in the glandular cells of gastric, duodenal, and rectal epithelium as well as endothelial cells and enterocytes of the small intestine. The virus can cause acute myocardial injury and chronic damage to the cardiovascular system. An acute cardiac injury was found in 12% of infected people admitted to the hospital in Wuhan, China, and is more frequent in severe disease. Rates of cardiovascular symptoms are high, due to the systemic inflammatory response and immune system disorders during disease progression, but acute myocardial injuries may also be related to ACE2 receptors in the heart. ACE2 receptors are highly expressed in the heart and are involved in heart function. A high incidence of thrombosis and venous thromboembolism has been found people transferred to intensive care unit with COVID-19 infections, and may be related to poor prognosis. Blood vessel dysfunction and clot formation (as suggested by high D-dimer levels caused by blood clots) are thought to play a significant role in mortality, incidences of clots leading to pulmonary embolisms, and ischemic events within the brain have been noted as complications leading to death in people infected with SARS-CoV-2. Infection appears to set off a chain of vasoconstrictive responses within the body, constriction of blood vessels within the pulmonary circulation has also been posited as a mechanism in which oxygenation decreases alongside the presentation of viral pneumonia. Furthermore, microvascular blood vessel damage has been reported in a small number of tissue samples of the brains – without detected SARS-CoV-2 – and the olfactory bulbs from those who have died from COVID-19. Another common cause of death is complications related to the kidneys. Early reports show that up to 30% of hospitalized patients both in China and in New York have experienced some injury to their kidneys, including some persons with no previous kidney problems. Autopsies of people who died of COVID-19 have found diffuse alveolar damage, and lymphocyte-containing inflammatory infiltrates within the lung.

PREVENTION

Preventive measure to reduce the chances of infection includes getting vaccinated staying at home, wearing a mask in public, avoiding crowded place, keeping distance from others ventilating indoor space, managing potential exposure duration washing hand with soap and water often and for a least 20 s practicing good respiratory hygiene, and avoiding touching the eyes nose or mouth with unwashed hand.

VACCINE

A COVID19 vaccine is a vaccine intended to provide acquired immunity against SARSCoV2, the virus causing COVID-19. Before the COVID-19 pandemic, there was an established body of knowledge about the structure and function of coronaviruses causing diseases such as SARS and MERS, which enabled accelerated development of various vaccine technologies during early 2020. On January 10, 2020, the SARS-CoV-2 genetic sequence data were shared through GISAID, and by March 19, the global pharmaceutical industry announced a major commitment to address COVID-19. In Phase III trials, several COVID19 vaccines have demonstrated efficacy as high as 95% in preventing symptomatic COVID19 infections. As of April 2021, 15 vaccines are authorized by at least one national regulatory authority for public use: two RNA vaccines (Pfizer–BioNTech and Moderna), six conventional inactivated vaccines (BBIBP-CorV, CoronaVac, Covaxin, WIBP-CorV, CoviVac, and QazVac), five viral vector vaccines (Sputnik Light, Sputnik V, Oxford–AstraZeneca, Convidecia, and Johnson and Johnson), and two protein subunit vaccines (EpiVacCorona and RBD-Dimer). In total, as of March 2021, 308 vaccine candidates are in various stages of development, with 73 in clinical research, including 24 in Phase I trials, 33 in Phase I–II trials, and 16 in Phase III development. Many countries have implemented phased distribution plans that prioritize those at highest risk of complications, such as the elderly, and those at high risk of exposure and transmission, such as health care workers. Single-dose interim use is under consideration to extend vaccination to as many people as possible until vaccine availability improves. As of May 18, 2021, 1.53 billion doses of COVID19 vaccine have been administered worldwide based on official reports from national health agencies. AstraZeneca anticipates producing 3 billion doses in 2021, Pfizer–BioNTech 1.3 billion doses, and Sputnik V, Sinopharm, Sinovac, and Johnson and Johnson 1 billion doses each. Modern targets producing 600 million doses and Convidecia 500 million doses in 2021. By December 2020, more than 10 billion vaccine doses had been reordered by countries, with about half of the doses purchased by high-income countries comprising 14% of the world's population.

FACE MASKS AND RESPIRATORY HYGIENE

Masks with an exhalation valve. The valves are a weak point that can transmit the viruses' outwards. The WHO and the US CDC recommend individuals wear non-medical face coverings in public settings where there is an increased risk of transmission and where social distancing measures are difficult to maintain. This recommendation is meant to reduce the spread of the disease by asymptomatic and pre-symptomatic individuals and is complementary to established preventive measures such as social distancing. Face coverings limit the volume and travel distance of expiratory droplets dispersed when talking, breathing, and coughing. A face covering without vents or holes will also filter out particles containing the virus from inhaled and exhaled air, reducing the chances of infection. However, if the mask includes an exhalation valve, a wearer that is infected (maybe without having noticed that, and asymptomatic) would transmit the virus outward through it, despite any certification they can have. Hence, the masks with exhalation valve are not for the infected wearers and are not reliable to stop the pandemic in a large scale. Many countries and local jurisdictions encourage or mandate the use of face masks or cloth face coverings by members of the public to limit the spread of the virus. Masks are also strongly recommended for those who may have been infected and those taking care of someone who may have the disease. When not wearing a mask, the CDC recommends covering the mouth and nose with a tissue when coughing or sneezing and recommends using the inside of the elbow if no tissue is available. Proper hand hygiene after any cough or sneeze is encouraged. Health-care professionals interacting directly with people who have COVID-19 are advised to use respirators at least as protective as NIOSH-certified N95 or equivalent, in addition to other personal protective equipment.

AVOIDING CROWDED INDOOR SPACES AND VENTILATION

Crowded indoor spaces should be avoided. When indoors, increasing the rate of air change, decreasing recirculation of air, and increasing the use of outdoor air can reduce transmission. The WHO recommends ventilation and air filtration in public spaces to help clear out infectious aerosols. Exhaled respiratory particles can build-up within enclosed spaces with inadequate ventilation. The risk of COVID-19 infection increases especially in spaces where people engage in physical exertion or raise their voice (e.g. exercising, shouting, and singing) as this increases exhalation of respiratory droplets. Prolonged exposure to these conditions, typically more than 15 min, leads to higher risk of infection.

HAND WASHING AND HYGIENE

Thorough hand hygiene after any cough or sneeze is required.[5-8] The WHO also recommends that individuals wash hands often with soap and water for at least 20 s, especially after going to the toilet or when hands are visibly dirty, before eating and after blowing one's nose. When soap and water are not available, the CDC recommends using an alcohol-based hand sanitizer with at least 60% alcohol. For areas where commercial hand sanitizers are not readily available, the WHO provides two formulations for local production. In these formulations, the antimicrobial activity arises from ethanol or isopropanol. Hydrogen peroxide is used to help eliminate bacterial spores in the alcohol; it is "not an active substance for hand antisepsis." Glycerol is added as a humectant.

SOCIAL DISTANCING

Social distancing (also known as physical distancing) includes infection control actions intended to slow the spread of the disease by minimizing close contact between individuals. Methods include quarantines; travel restrictions; and the closing of schools, workplaces, stadiums, theaters, or shopping centers. Individuals may apply social distancing methods by staying at home, limiting travel, avoiding crowded areas, using no contact greetings, and physically distancing themselves from others. Many governments are now mandating or recommending social distancing in regions affected by the outbreak. Outbreaks have occurred in prisons due to crowding and an inability to enforce adequate social distancing. In the United States, the prisoner population is aging and many of them are at high risk for poor outcomes from COVID-19 due to high rates of coexisting heart and lung disease, and poor access to high-quality health care.

SURFACE CLEANING

After being expelled from the body, coronaviruses can survive on surfaces for hours to days. If a person touches the dirty surface, they may deposit the virus at the eyes, nose, or mouth where it can enter the body and cause infection. Evidence indicates that contact with infected surfaces is not the main driver of COVID-19, leading to recommendations for optimized disinfection procedures to avoid issues such as the increase of antimicrobial resistance through the use of inappropriate cleaning products and processes. Deep cleaning and other surface sanitation have been criticized as hygiene theatre, giving a false sense of security against something primarily spread through the air. The amount of time that the virus can survive depends significantly on the type of surface, the temperature, and the humidity. Coronaviruses die very quickly when exposed to the UV light in sunlight. Like other enveloped viruses, SARS-CoV-2 survives longest when the temperature is at room temperature or lower, and when the relative humidity is low (<50%). On many surfaces, including as glass, some types of plastic, stainless steel, and skin, the virus can remain infective for several days indoors at room temperature, or even about a week under ideal conditions. On some surfaces, including cotton fabric and copper, the virus usually dies after a few hours. As a rule of thumb, the virus dies faster on porous surfaces than on non-porous surfaces. However, this rule is not absolute, and of the many surfaces tested, two with the longest survival times are N95 respirator masks and surgical masks, both of which are considered porous surfaces. The CDC says that in most situations, cleaning surfaces with soap or detergent, not disinfecting, are enough to reduce risk of transmission. The CDC recommends that if a COVID-19 case is suspected or confirmed at a facility such as an office or day care, all areas such as offices, bathrooms, common areas, and shared electronic equipment such as tablets, touch screens, keyboards, remote controls, and ATM machines used by the ill persons should be disinfected. Surfaces may be decontaminated with 62–71% ethanol, 50–100% isopropanol, 0.1% sodium hypochlorite, 0.5% hydrogen peroxide, and 0.2–7.5% povidone-iodine. Other solutions, such as benzalkonium chloride and chlorhexidine gluconate, are less effective. Ultraviolet germicidal irradiation may also be used. A datasheet comprising the authorized substances to disinfection in the food industry (including suspension or surface tested, kind of surface, use dilution, disinfectant, and inoculum volumes) can be seen in the supplementary material of.

SELF-ISOLATION

Self-isolation at home has been recommended for those diagnosed with COVID-19 and those who suspect they have been infected. Health agencies have issued detailed instructions for proper self-isolation. Many governments have mandated or recommended self-quarantine for entire populations. The strongest self-quarantine instructions have been issued to those in high-risk groups. Those who may have been exposed to someone with COVID-19 and those who have recently travelled to a country or region with the widespread transmission have been advised to self-quarantine for 14 days from the time of last possible exposure.

HEALTHY DIET AND LIFESTYLE

The Harvard T.H. Chan School of Public Health recommends a healthy diet, being physically active, managing psychological stress, and getting enough sleep. There is no good evidence that Vitamin D status has any relationship with COVID-19 health outcomes.

MECHANISM OF ACTION FOR COVID-19

Human has long been infected by coronavirus as it is one of those responsible for the common cold. It is a contagious viral infection that can be spread through inhalation or ingestion of viral droplets as a result coughing and sneezing and touching infected surface are primary sources of infection. The coronavirus genome is comprised of ~30,000 nucleotides. It encodes four structural proteins, nucleocapsid (N) protein, membrane (M) protein, spike (S) protein and envelop (E) protein, and several non-structural proteins (nsp) [Figure 1]. The capsid is the protein shell, inside the capsid, there is nuclear capsid or N-protein which is bound to the virus single positive strand RNA that allows the virus to hijack human cells and turn them into virus factories. The N protein coats the viral RNA genome which plays a key role in its replication and transcription. The N-terminal of the N protein which is binding to genomic and sub-genomic RNAs in MHV and IBV virions and process the viral replication and transcription. This is one of the important open research problems developing of an effective drug targeting to prevent the contacts between N-terminal of N-protein and single-positive RNA strand which can stop viral replication and transcription. Sarma *et al*. (2020) reported that two important class of compounds, theophylline and pyrimidone drugs as possible inhibitors of RNA binding to the N terminal domain of N protein of coronavirus, thus opening new avenues for *in vitro* validations.

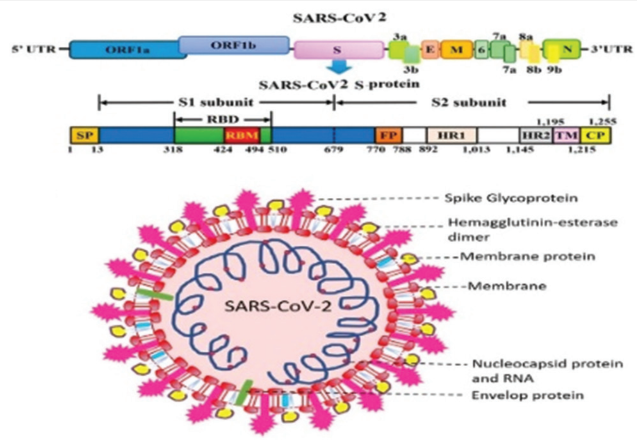
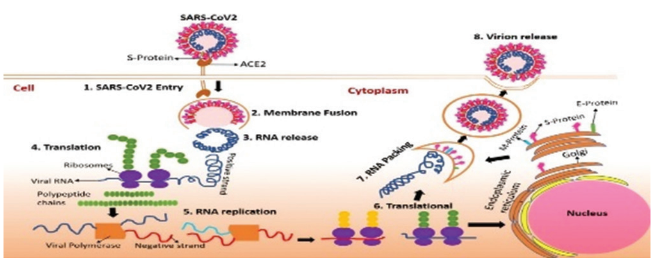


Figure 1: (a) Schematic representation of the genome organization and functional domains of S protein for COVID-19. The single-stranded RNA genomes of COVID-19 encode two large genes, the ORF1a and ORF1b genes, which encode 16 non-structural proteins (nsp1–nsp16). The structural genes encode the structural proteins, spike (s), envelope (e), membrane (m), and nucleocapsid (n). The accessory genes denoted in shades of green. The structure of S protein is shown beneath the genome organization. The S protein is consisting of the S1 and S2 subunits. The S1/S2 cleavage sites are highlighted by dotted lines. In the S protein, cytoplasm domain (CP); fusion peptide (FP); heptad repeat (HR); receptor-binding domain (RBD); signal peptide (SP); and transmembrane domain (TM) are shown (b) the viral surface proteins, spike, envelope, and membrane, are embedded in a lipid bilayer. The single-stranded positive-sense viral RNA is associated with the nucleocapsid protein. The M protein is most abundant in the viral surface and it is believed to be the central organizer for the coronavirus assembly. The S protein is integrated over the surface of the virus, it mediates attachment of the virus to the host cell surface receptors and fusion between the viral and host cell membranes to facilitate viral entry into the host cell (Kirchdoerfer *et al*.). The E protein is a small membrane protein composed ~76 to 109 amino acid and minor component of the virus particle, it plays an important role in virus assembly, membrane permeability of the host cell, and virus-host cell interaction (Gupta *et al*., 2020). A lipid envelop encapsulates the genetic material. Hemagglutinin-esterase dimer (HE) has been located on the surface of the viral. The HE protein may be involved in virus entry, is not required for replication, but appears to be important for infection of the natural host-cell (Lissenberg *et al*., 2005). State-of-the-art cryo-EM experiments have revealed the full structure of the spike (s) protein in the close (pdb id: 6VXX) (Walls *et al*., 2020) and open (pre-fusion) states (pdb id: 6VYB) (Wrapp *et al*., 2020). Such glycoprotein is made of three identical chains with 1273 amino acid each and it is composed by two well-defined protein domain regions: S1 and S2 subunits which are associated to cell recognition and the fusion of viral and cellular membranes, respectively. The latter process occurs through different protein conformational changes that remain still uncharacterized.

The mechanism of viral entry and replication and RNA packing in the human cell is mapped. The coronavirus spike (S) protein attaches to ACE2 receptors that are found on the surface of many human cells, including those in the lungs allowing virus entry. The coronavirus S protein is subjected to proteolytic cleavages by host proteases (i.e. trypsin and furin), in two sites located at the boundary between the S1 and S2 subunits (S1/S2 site). In a later stage happens the cleavage of the S2 domain (S2′ site) to release the fusion peptide. This event will trigger the activation of the membrane fusion mechanism. Searching for antibodies can find support on molecular targeting which can utilize the structural information (a sequence) of the binding region which is found in angiotensin-converting enzyme 2 receptor. In this way, this protocol could device a treatment to block the viral entry. Typically, human cell ingests the virus in a process called endocytosis. Once entered the cytoplasm, it has been suggested most likely that COVID-19 employs a unique three-step method for membrane fusion, involving receptor binding and induced conformational changes in spike (S) glycoprotein followed by cathepsin L proteolysis through intracellular proteases and further activation of membrane fusion mechanism within endosomes (Simmons *et al*., 2005). Then, the endosome opens to release virus to the cytoplasm, and uncoating of viral nucleocapsid (N) is started through proteasomes which typically can hydrolyze endogenous proteins, but they are also capable of degrading exogenous proteins such as the SARS nucleocapsid protein (Wang *et al*., 2010). A different two-step mechanism has been suggested (Li, 2016) and in this case, the virion binds to a receptor on the target host cell surface through its S1 subunit and the spike is cleaved by host proteases (Hasan *et al*., 2020) and then it is expected the fusion at low pH between viral and host target membranes through S2 subunit. Finally, the viral genetic material a single-stranded RNA is fully released into the cytoplasm. There takes place the replication and transcription processes which are mediated by the so-called replication/transcription complex (RTC). Such complex is encoded in the viral genome and it is made of nsp. The RTC is believed to induce double-membrane structures in the cytoplasm of the infected cell (Van Hemert *et al*., 2008). Following the positive RNA genome is translated to generate replicase proteins from open reading frame 1a/b (ORF 1a/b) [Figure 1]. These proteins use the genome as a template to generated full-length negative sense RNAs, which subsequently serve as templates in generating addition full-length genomes. Structural viral proteins, M, S, and E are synthesized in the cytoplasm and then inserted into the endoplasmic reticulum (ER) [Figure 2], and transfer to ER-Golgi intermediate compartment (ERGIC) (Masters, 2006; Song *et al*., 2004). Furthermore, in the cytoplasm, nucleocapsids are formed from the encapsulation of replicated genomes by N protein, and as a result, they coalesce within the ERGIC membrane in order to self-assembly into new virions. Finally, novel virions are exported from infected cells by transport to the cell membrane in smooth-walled vesicles and then secreted through a process called exocytosis so that can infect other cells. In the meantime, the stress of viral production on the ER eventually leads to cell death. However, the mechanism of action for novel COVID-19 is still unknown (Masters, 2006).[9-29]

The schematic diagram of the mechanism of COVID-19 entry and viral replication and viral RNA packing in the human cell.



CONCLUSION

There are hundreds of coronaviruses, most of which circulate in animals. Only seven of these viruses infect human and four of them cause symptoms of the common cold. However, 3 times in the past 20 years a coronavirus have jumped from animals to human to cause severe disease. COVID-19, a new and sometimes deadly respiratory illness that is believed to have originated in a live animal market in China, has spread rapidly throughout that country and the world. The new coronavirus was first detected in Wuhan, China in December 2019. Tens of thousands of people were infected in China, with the virus spreading easily from person to person in many parts of country. Health officials in the United States and around the world are working to contain the spread of the virus through public health measure such as social distancing, contact tracing, testing, quarantines, and travel restrictions. Scientist is working to find medication to treat the disease and to develop a vaccine. Public health measure like ones implemented in China and now around the world will hopefully blunt the spread of the virus while treatment and a vaccine is developed to stop it.

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