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GLOBAL EPIDEMIC OF CORONAVIRUS—COVID-19: WHAT CAN WE DO TO MINIMIZE RISKS

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ABSTRACT
The 2019 coronavirus outbreak started in Hubei Province in China. Despite major travel restrictions, the virus spread across all China's provinces. Based on the rapidity of the dispersion, coronavirus has become a serious public health concern in China and a few other countries. Coronavirus belongs to a large family of viruses that usually affect wild animals. Following gene mutations and with close exposure to infected animals, these viruses occasionally are transmitted to humans and subsequently spread among humans. Coronaviruses cause the common cold and more severe diseases, such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). Such diseases are infectious at close range and spread via person-to-person contact, with an approximate death rate of 3%. An effective vaccine against the 2019/20 coronavirus is expected to be available within 6 months. Precautions taken to prevent the spread of the coronavirus are is similar to those used to lessen transmission of the common cold and flu-like illnesses, but more stringent quarantining is requiring. Apart from wearing facemasks, social distancing, limiting time in public places and transportation, frequent washing hands with any soap in running water are essential to prevent its spread. COVID-19 is going to be a global problem: economically, socially, and a pandemic. This article is intended top rovide a general description of the current situation related to the COVID-19 outbreak and not to provide medical advice.
KEYWORDS: Epidemic; Pandemic; H5N1; SARS; MERS; COVID-19; Zika.

INTRODUCTION

The current outbreak of coronavirus—named COVID-19 (previously names as 19 or Wuhan coronavirus—originated in Wuhan city, in China's Hubei Province.[1] Despite major travel restrictions, the virus rapidly spread to other provinces within China and later to neighboring and also to distantly located countries because of international travel. By definition, it has become an epidemic.[2] Travelers should be concerned about this outbreak, in part because of the potential of travel-related exposure to the virus and flight cancellations that can affect business and holiday schedules and travel plans.

In December 2019, Chinese health authorities first reported to the World Health Organization (WHO) a cluster of persons with a viral-mediated unusual form of severe pneumonia. Individuals with preexisting disorders, especially ones affecting the immune system, and those taking medications such a prednisolone or a similar category of medications that suppress the immune system are more vulnerable to develop severe forms of the disease, pneumonia, and death.

It is important that the WHO, Hubei province health department, United States Centers for Disease Control (US, CDC), and China's Center for Disease Control and Prevention (CCDC) work in collaboration to share data and provide frequent updates and advice to the other countries for the benefit of the public.[3] Among other means, this should include sharing reliable information and guidance through social media platforms. This is particularly important because a few independent media outlets have disseminated exaggerated claims and outrageous predictions. For example, one Australian outlet, in the absence of any scientific data, reported that the Wuhan coronavirus epidemic would lead to more than 65 million human deaths.[4]

Characteristics and evolution of coronavirus (COVID-19)?

A variety of coronaviruses have been identified, especially those causing common colds and other upper respiratory infections. Coronaviruses have been in existence for a long time and are abundant among wild animals. Based on genetic glycoprotein analyses, the main reservoir for COVID-19 in nature has been identified as bats (similar to rabies in many countries),

whereas snakes and other animals can also be carriers: these animals act as a reservoir for such viruses.

When certain exotic live wild animals and their flesh were brought to animal markets to sell, as occurred in Wuhan, the disease began to spread to humans (i.e., become a zoonotic disease. This virus might have mutated and has acquired the capacity to spread to humans and then from human to human). The imposed strict travel restrictions were an attempt to control the spread of the virus within China and were appropriate.

January 2020, the World Health Organization *temporarily* named the new virus the 2019 novel coronavirus (COVID-19).[5] The COVID-19 name was announced the second week of February. COVID-19 has a genome structure typical for that of a coronavirus and genetically related to Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS). It belongs to the cluster of beta coronaviruses, including bat SARS-like (SL)-ZC45, bat SL-ZXC21, SARS-CoV, and MERS-CoV.[6]

The gene sequences of COVID-19 reported (see Genbank) confirmed that it is a single-stranded, positive-sense RNA (+ssRNA) (~30 kb) with 5'-cap structure and 3'-poly-A tail, which is the same genome size of CoV (~30 kb)].[6] The appearance of COVID-19 is illustrated in Figure 1. Coronavirus-related pneumonia leads to the massive production of a variety of inflammatory cytokines, including TNFα (available on Virological.org) that significantly worsen the outcome.

To make the article attractive, you may consider including following figures in the manuscript.

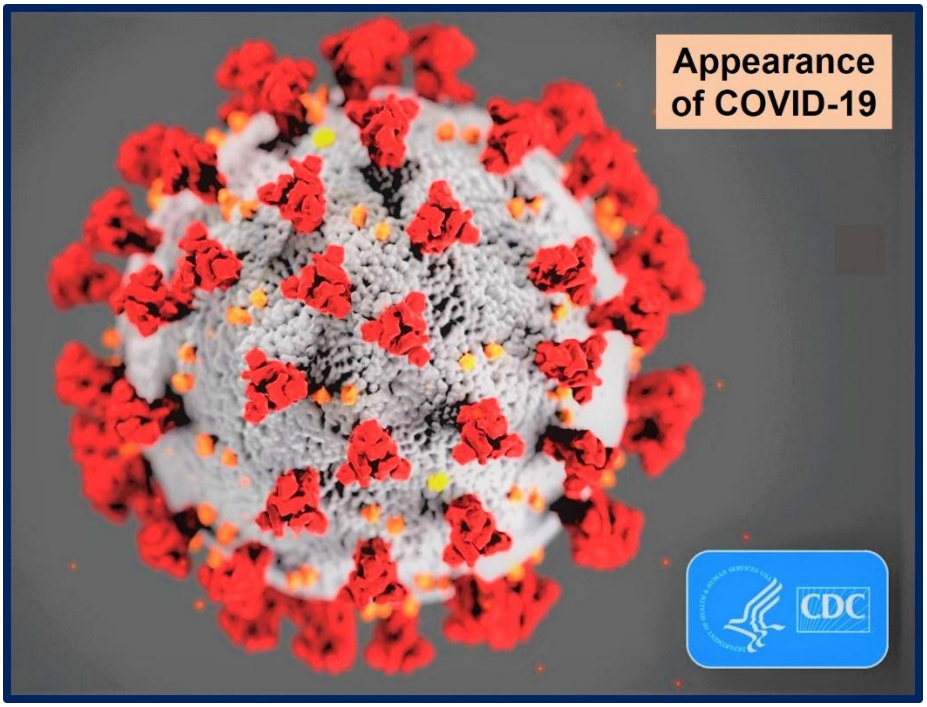

Figure 1:
The appearance of COVIC-19. From Center for Disease Control and Prevention, USA: https://www.cdc.gov/coronavirus/2019-ncov/index.html

When a certain gene mutation occurs within the virus genome, the virus acquires the capacity to spread to humans (zoonosis) and also between humans. It might mutate again in due course, either decreasing or increasing its virulence. Viral recombination and transmission may have occurred following direct contact of live wild animals or flesh or the consumption of raw or partially cooked meat from infected animal; this could enable transfer of the virus to humans, as apparently happened in the Wuhan epidemic.

Similarity of COVID-19 and a comparison with other common viruses

COVID-19 is a part of a family of coronaviruses that includes the common cold, SARS, and MERS.[5] MERS was first identified in Saudi Arabia in 2012, and around 34% of infected people died (i.e., 858 of 2,494 cases). The SARS outbreak led to 8,098 identified cases and 774 deaths (9.6%). In 2002/03, the SARS epidemic quickly subsided. COVID-19 is less virulent than MERS.[7] The proposed schematic structure of COVID-19 is illustrated in Figure 2.

Figure 2

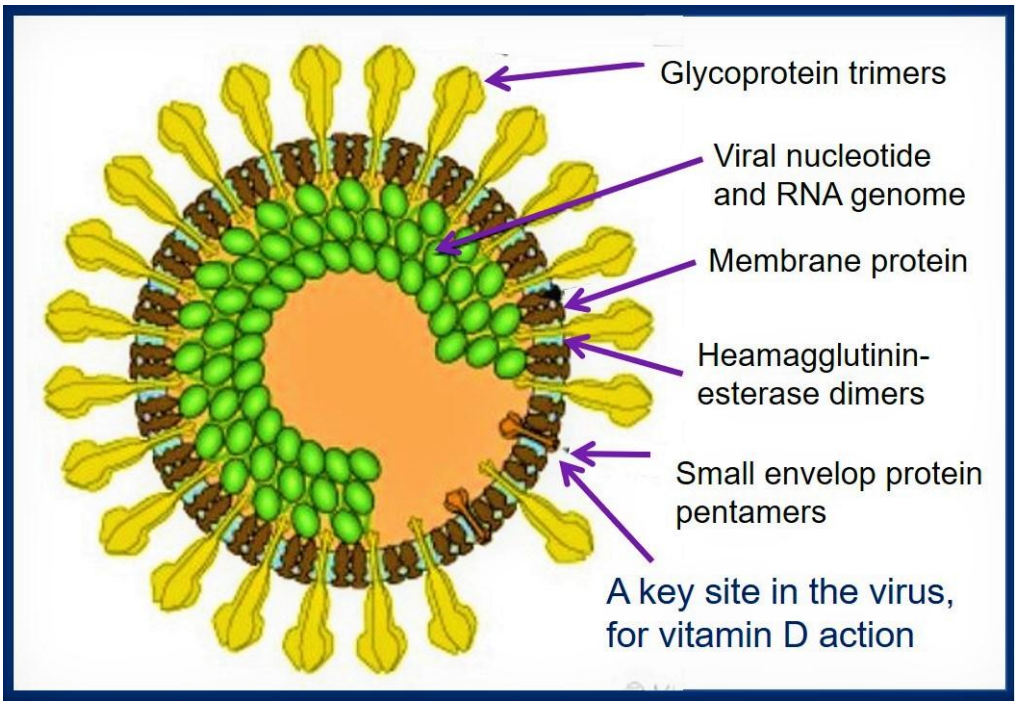

Figure 2: Generic structure of coronaviruses, including COVID19. Adapted from Viral Zone-2020: Swiss Institute f of Bioinformatics, C.M.U., 1 rue Michel-Servet, 1211 Geneve 4, Switzerland (https://www.sib.swiss/about-sib/news/10643-sib-experts-and-resources-in-the-fight-against-coronavirus).

The Wuhan coronavirus is considered moderately infectious and somewhat similar to SARS, which caused an epidemic in China in 2003. Infectiousness determines how easily and rapidly a virus is transmitted from person to person. In the absence of proper precautions, based on the contact information, it has been estimated that one person with the Wuhan coronavirus could infect as many as four people through a single exposure event. Patients with this disease are now reported in Europe, Japan, Singapore, Taiwan, South Korea, Thailand, Canada, Sri Lanka, and the United States—more than 25 countries so far. For updated information, please see the CDC and WHO websites: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.

The following provides a virus name, the year of identification, and the reported death rate of other communicable viral epidemics in the recent past: Marburg (first identified in 1967; fatality rate 80%); Ebola (1976; 40%); Hendra (1994; 57%); H5N1-bird flu (1997; 53%); Nipah (1998; 77%); SARS (2002; 9.6%); H1N1 (2009; 17.4%); MERS (2012; 34.4%); H7N9 (bird flu) (2013; 39.3%); COVID-19 (2019; ~3.0%) (based on CDC and WHO data).

Incubation periods of COVID-19 and other recent viral outbreaks

Common diseases such as the cold and influenza are infectious to others for a period of 2 to 6 day. Although there may not be obvious signs and symptoms present during the incubation period, persons can still spread the virus during that time. Cough-associated droplets carry infectious virus particles that spread the disease to those who are nearby, especially when an infected person travels, such as in public transportation or air travel. Because of the potential of the wide spread of infectious particles, it is difficult to isolate undiagnosed people with such viruses.

A person who has been or is suspected of having been exposed or is in the incubation period should be quarantined and observed in a secure location. It is estimated that the incubation period, the time from infection to the manifestation of signs and symptoms of the Wuhan coronavirus, can be between 4 and 14 days. Because of this uncertainty and the lack of clear-cut manifestations, such as are seen in cases of measles and chicken pox, coronavirus infections can go unnoticed throughout the entire incubation period. A quarantine period for COVID-19 has been established as 14 days to assure the virus does not spread to others. This is a standard measure carried with other diseases, such as Ebola and similar viral illnesses, to prevent infecting others.

Symptoms of COVID-19

The symptoms of COVID-19 generally consist of cough, mild fever, and shortness of breath. However, these symptoms are similar to those of the common cold and flu, so it is difficult to separate those with the illness by signs and symptoms alone. However, serology can be used to confirm the diagnosis of COVID-19. A smaller number of infected people could present with non-respiratory symptoms, such as nausea, vomiting, or diarrhea, similar to those associated with enteric viruses.

Most people affected with COVID-19 recover within a few days with symptomatic and supportive therapy. However, a small minority of people, especially those with immune compromised status, those taking medications such as prednisolone, and infants and the elderly, may experience serious infection, such as infective bronchitis or severe pneumonia, and perhaps secondary bacterial infections, which make their cases worse.[5]

Contagiousness of coronavirus

COVID-19 is a respiratory virus that spreads through the air, touch, and personal contact. Thus, exposure to affected people in crowded places, public transportations systems, and air travel are the most common routes of acquiring this disease. Coronaviruses can travel wrapped in droplets that are produced when an infected person breathes, talks, coughs, or sneezes. These particulate droplets are suspended in the air. Because these droplets are a little heavier than other virus types, in general they travel only as far as about 6 feet before scattering.

To acquire the Wuhan coronavirus, one needs to be in close contact with a person infected with the coronavirus for a period. In the absence of such a close contact, encounters such as visiting a shopping center are unlikely to lead to contracting this disease. In contrast, measles or varicella (chicken pox) spread through smaller droplets that spread over much greater distances and are highly infectious. Thus, comparatively, the infectivity is less with COVID-19 virus. Coronaviruses can also be present in the stools of affected individuals. However, transmission via the fecal–oral route is less likely.

There are no approved or effective antiviral medications or vaccines available for COVID-19. Thus, the current treatment is supportive therapy and keeping affected persons comfortable while they achieve natural recovery. A small number of people with high viral loads and/or compromised immune systems are likely to need to be cared for in an intensive care units (ICUs).

Protective face masks against viruses

A respirator mask (disposable particulate respirator) is a personal protective device that is worn on the face, covering the nose and mouth. Some of the face masks currently sold (online or in stores), unless designed specifically to filter smaller particles such as viruses, are unlikely to prevent the inhalation of COVID-19 or any other viruses. Respirator face mask types are rated and certified by the National Institute for Occupational Safety and Health (NIOSH), the CDC, and the Occupational Safety and Health Administration (OSHA).

NIOSH-approved disposable respirators are rated as: **N** = **N**ot resistant to oil; **R** = **R**esistant to oil; and **P** = strongly resistant (oil **P**roof). As per OSHA, any of these three types of masks can be used to filter virus particles and other particulate matter in the air. There are nine types of disposable particulate respirators. For more information, please visit https://www.osha.gov/SLTC/etools/respiratory/index.html. For non-affected people, the use of a respirator with an exhalation valve is more tolerable and easier to use.

In circumstances when one is not in close contact with an infected person or traveling in crowded places, the CDC does not recommend wearing face masks. However, when the use is indicated, it is recommended that individuals use a mask/respirator with one of the following ratings: N95, N99, R95, or R99. Although P100 masks are effective, they are uncomfortable to use in normal travel circumstances. The rating numbers indicate the percentage of filtering efficiency of particles, such as viruses.

Commonsense measures to prevent infection

During the winter, people are much more likely to get influenza B (the flu) than any other viral disease. Those who have immune suppression or who lack optimal immune protective activity are more likely to contract viral diseases. Precautions to be taken to prevent the spread of COVID-19 are similar to those for preventing the contraction of other common viral diseases. Healthy people who are not in close contact with a person with Wuhan coronavirus (COVID-19) are unlikely to be at risk for the disease.

Following the basic infectious disease prevention principles against air-borne diseases generally is sufficient to curtail the spread of COVID-19. Such principles include avoiding crowded places employing regular hand washing with soap and water and using medical grade hand sanitizers (an alcohol-based disinfectant that contains at least 60% alcohol) and covering the nose and mouth with disposable tissues or your inner elbow when coughing or sneezing.

Additional actions one could take to minimize infections are described on the CDC website.[8] Because coronaviruses can enter the body via mucosal surfaces, one should not touch eyes, nose, or mouth without first washing hands thoroughly. Therefore, it is advisable to wash hands thoroughly with soap and water for at least 20 seconds when returning home. Measures such as staying at home when one has flu-like symptoms and/or an unexplained fever and keeping distance from people who have signs of a respiratory tract infection, including runny nose, coughing, and sneezing, should be followed to minimize the risks of viral respiratory diseases.

In contrast to COVID-19, highly infectious viral diseases, such as measles and chicken pox, and bacterial diseases, such as tuberculosis, are organisms that can travel through the air or via droplets for more than 100 feet, and thus could infect many more people than does COVID-19. Other viruses, such as HIV and hepatitis, are transmitted only through direct contact with the bodily fluids of an infected person.

Human-to-human transmission of COVID-19

Human-to-human transmission can be curtailed by taking efficient public health measures, such as well-organized tracking of individuals who had been in contact with an infected person, isolating sick people (quarantine measures), and large-scale public education. Measures such as mandatory temperature checking and health screenings of suspected persons at major airports, especially those arriving from Wuhan and other affected regions in China, are helpful in the early identification and quarantining of people with illness.

Health authorities in many countries have taken effective public health measures to curtail this disease, which is having a tangible impact on curtailing the spread of COVID-19. With the rapid implementation of efficient public health measures, many countries have been successful in controlling the spread of COVID-19. Failure to take effective precautionary actions is likely to be deleterious for the populous and the country's economy.

Dissemination of the disease via air travelers

The spread of COVID-19 to countries outside China has occurred primarily from air travel of Chinese tourists and workers and visitors returning home from Wuhan and other infected regions in China. In countries such as the United States, individuals arriving from areas where the coronavirus is present are strictly quarantined for a period of two weeks to ensure that they are not infectious. From such travelers, others can get infected even though they may not have visited the places known to have widespread disease. Thus, quarantine is an essential part of public health measures.

The number of people infected with the Wuhan coronavirus in China has exponentially increased over the past few weeks, faster than occurred with the SARS virus (SARS-CoV). Nevertheless, the average person should not panic, and there is no reason to cancel travel plans of otherwise healthy people, except to avoid visiting any part of China and a few cities that might have been affected. However, there is a possibility that this restriction might be extended to other regions and countries if the disease continues to spread. When new information becomes available, key global public health organizations, such as the CDC, WHO, and similar organizations in China, should issue updated guidance and additional steps required to prevent disease spread.

Mortality due to COVID-19

Currently, the estimated death rate associated with Wuhan coronavirus is approximately 3%, which is tenfold less than that with the SARS virus. However, if the virus acquires further mutations, its virulence can change. Intensive supportive therapies and ICU-based care for boosting the immune system in those who are experiencing significant respiratory symptoms, including pneumonia, can reduce deaths.

Many might be infected with the coronavirus, but if their immune systems are not compromised, they may never even recognize that they have had this virus and may experience full recovery with only mild illness, yet they can be infectious to others. Considering this, the incidence and true prevalence of the Wuhan coronavirus can be markedly underestimated. It is also possible that deaths caused by COVID-19 are underestimated because the cause of death could be documented as other disease, such as bronchitis or pneumonia unrelated to coronavirus.

How long will it take to develop a vaccine?

In general, the development of an effective vaccine for a respiratory viral disease takes at least one year. By the time a good vaccine is developed, the current coronavirus outbreak is likely to be over. For the SARS outbreak in 2003, it took 20 months to develop a vaccine that was ready for human clinical trials. However, by that time, the disease was well under control.

In contrast, it took only 6 months to develop a vaccine for the Zika virus, for which an outbreak occurred in 2015. The author estimates that researchers will generate an effective vaccine for the current coronavirus in about 6 months. In recent work, the genome of the coronavirus has been sequenced and candidate proteins have been identified that can be used for the generation of a vaccine.

Chloroquine is a widely used against malaria and autoimmune diseases and is also known to block fusion of viruses and interfering with glycosylation, as in the case of SARS-CoV cellular receptors.[9] Antiviral drugs, such as ribavirin, interferon, lopinavir-ritonavir, as well as corticosteroids have been studied in patients with SARS or MERS, although the efficacy of some drugs remains a matter of controversy.[10] Remdesivir is a novel antiviral drug in the class of nucleotide analogs.

A recent *in vitro* study reported that the combination of chloroquine and remdesivir is effective in the control of COVID-19 infection. Preliminary data using animal models suggest that broad-spectrum antivirals, such as an RNA polymerase inhibitor, remdesivir and lopinavir/ritonavir and interferon-β might be effective against COVID-19, and previously was reported to be effective against MERS-CoV. Thus, researchers are experimenting with the use of nucleic acid vaccine platform approaches that have been used for generating vaccines against SARS-CoV and MERS-CoV.

What can be done right now to reduce disease risk and severity?

With severe infections of coronaviruses, the following are needed: diagnosis of disease at the earliest possible time, isolation of patients and reporting to authorities for surveillance, the provision of supportive treatments, and the provision of dynamic guidance to avoid unnecessary panic. For individuals, good personal hygiene, a fitted

mask, ventilation, and avoiding crowded places will help prevent the spread of COVID-19 infection.

Clothe, masks, and surfaces impregnated with ionic zinc oxide (Zno; Zn^{2+}–O^{2-}) nanoparticles[11] with wurtzite structure or perhaps PEGylated ZnO-nano-particles[12] (or oxozinc) likely to have effective antibacterial and antiviral efficacy.[13, 14] Proper incorporation of ZnO-nanoparticles into materials can make them stable and able to kill pathogens on contact.[15] Preliminary data suggest that 2019-nCoV enters pulmonary cells via angiotensin 2 (ACE-2) and blocks the enzyme that degrade angiotensin II.[16] Resultant excess local concentration of angiotensin II causes pulmonary hypertension and edema, acute respiratory distress syndrome, and pneumonia-associated death. This pathway would allow opportunities to interfere with the progress of this disease.

Adequate vitamin D levels have been associated with reduced incidence and severity of enveloped viruses such as herpes zoster, Epstein-Barr, hepatitis, Ebola, HIV, dengue, measles, and mumps.[17, 18] Studies have reported the administration of an oral dose of 50,000 IU of vitamin D reduces the risks of having influenza. Vitamin D adequacy also reduces the severity of pneumonia, which is associated with coronavirus infections. Vitamin D is a natural vitamin, so the risk of administering too much is minuscule.

Those who are micronutrient deficient, especially those with hypovitaminosis D, are at a greater risk of developing viral diseases, including coronaviruses. Thus, the most effective option is to take higher doses of vitamin D supplements (now) and/or exposure to summer-like sun to bring serum 25(OH)D concentrations above 30 ng/mL (see next paragraph) to boost immunity before exposure. This approach should reduce the risk not only of coronavirus but also of the common cold, influenza, and associated pneumonia, thus reducing deaths.

Use of high-dose oral vitamin D and antioxidants to reduce the risks and severity of coronavirus infection

Vitamin D is known to improve the immune system, and vitamin D deficiency increases vulnerability to viral infections, such as colds.[17, 18] Especially during the winter months, unless supplements are taken, serum 25(OH)D concentrations are low in most people. Levels begin to rise only at the beginning of the summer. Considering its many biological and physiological aspects, the immunoregulatory and stimulation effects of vitamin D occur via several mechanisms.[17] The author thinks that vitamin D adequacy would help control and reduce the risks and severity of Wuhan coronavirus and similar viruses. It is advisable to maintain serum 25(OH)D concentrations in excess of 30 ng/mL (75 nmol/L), preferably at a level greater than 40 ng/L (100 nmol/L), together with sufficiency of other micronutrients, such as zinc, selenium, and antioxidants.

Considering the inability to diagnose COVID-19 during its several-day incubation period, people feeling not well who has fever, or has been exposed to an infected person should be self - quarantine or quarantined at a secure facility, where person will not get infect-ed from others.

They will be benefited from taking an oral loading dose of vitamin D of between 200,000 and 300,000 international units (IU) [four to six, 50,000 IU capsules] as a single *oral* dose, along with mentioned micro-nutrients supplementats, to strengthen the immunesystem. This can be repeated after one week to build up the body stores of vitamin D. This process would allow, rapidly achieving vitamin D sufficiency, and thus, the ability to strengthen the immune and other body-systems within 3 to 5 days of administration. This highly cost-effective therapy, cost no more than $5 per person, is expected to reduce the risks of contracting the disease/ COVID-19. If the person experienced the disease, he or she would have a milder disease with less complications, and a speedy recovery.

A single high dose or a higher doses taken a week apart, as described, can be administered in hospitals or in community or home settings. From a disease prevention strategy point of view, the most cost-effective approach would be the prophylactic administration of high-dose vitamin D to the entire community at risk before the coronavirus/COVID-19 appears in that locality or at an earliest possible time point.

Recently, the number of people infected with the coronavirus (COVID-19) in China has exponentially increased over the past few weeks, faster than occurred with the SARS virus (SARS-CoV). Nevertheless the current death rate from COVID-19 is much less than that of SARS or MERS. It is likely that not only this epidemic will be under control soon but also an effective vaccine will be available within next four to six months.

Such short-term administration of vitamin D is safe. In general, to cause adverse effects from orally-administered vitamin D, one needs to take daily doses of higher than 25,000 IU for many months or take 1 million IU daily for a f ew days. Thus, the mentioned doses will not cause adverse effects. Potential benefits from a high-dose oral vitamin D is far outweigh any theoretical risks.

An average person who is not directly exposed to an infected person should not panic. Media is portraying an exaggerated gloomy picture, but the acute situation will be over in few months. However, the socio-economic consequences, especially for China and for the global economy, will continue for a longer period. Things are likely to get much worse, before it starting to get better. In addition, flight cancellations and the travel restrictions are likely to be extended outside the China, as the disease continues to spread globally to become a pandemic soon.

Conflicts of Interest

The author declares no conflict of interests. He received no funding for this work or assistance in professional writing for this article.

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