

Current updates on COVID-19 - A review

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ABSTRACT

Coronaviruses are a family of viruses that cause illness such as respiratory diseases or gastrointestinal diseases. Respiratory diseases can range from the common cold to more severe diseases. A novel coronavirus outbreak was first documented in Wuhan, Hubei Province, China in December 2019. The World Health Organization (WHO) has declared the coronavirus disease 2019 (COVID-19) a pandemic. A global coordinated effort is needed to stop the further spread of the virus. A novel coronavirus (nCoV) is a new strain that has not been identified in humans previously. Once scientists determine exactly what coronavirus it is, they give it a name (as in the case of COVID-19, the virus causing it is SARS-CoV-2).



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INTRODUCTION

History of Coronavirus

COVID-19 is a disease caused by a new strain of coronavirus. **'CO' stands for corona, 'VI' for virus, and 'D' for disease.** Formerly, this disease was referred to as '2019 novel coronavirus' or '2019-nCoV

A novel coronavirus outbreak was first documented in Wuhan, Hubei Province, China in December 2019. As of this writing, it has now been confirmed on six continents and in more than 100 countries. As the world's health systems funnel resources into

learning about, treating, and preventing infections in humans, new information is released daily.

In this two-part article series, we will first provide some history on coronaviruses to put this disease outbreak in perspective, and discuss global health security and planning for pandemic response. Secondly, we will offer guidance from the best trusted sources for prevention and planning in the workplace and at home.

Two other recent coronavirus outbreaks have been experienced. Middle East Respiratory Syndrome (MERS-CoV) of 2012 was found to transmit from dromedary camels to humans. In 2002, Severe Acute Respiratory Syndrome (SARS-CoV) was found to transmit from civet cats to humans.

Although COVID-19 has already shown some similarities to recent coronavirus outbreaks, there are differences and we will learn much more as we deal with this one. SARS cases totalled 8,098 with a fatality rate of 11 percent as reported in 17 countries, with the majority of cases occurring in southern mainland China and Hong Kong (Figure 1).

The fatality rate was highly dependent on the age of

the patient with those under 24 least likely to die (one percent) and those over 65 most likely to die (55 percent). No cases have been reported worldwide since 2004.

According to the World Health Organization (WHO), as of 2020, MERS cases total more than 2,500, have been reported in 21 countries, and resulted in about 860 deaths.³ The fatality rate may be much lower as those with mild symptoms are most likely undiagnosed.

Only two cases have been confirmed in the United States, both in May of 2014 and both patients had recently travelled to Saudi Arabia.

Most cases have occurred in the Arabian Peninsula. It is still unclear how the virus is transmitted from camels to humans.

Its spread is uncommon outside of hospitals. Thus, its risk to the global population is currently deemed to be fairly low [1].

COVID-19

The World Health Organization (WHO) has declared the coronavirus disease 2019 (COVID-19) a pandemic.

A global coordinated effort is needed to stop the further spread of the virus.

A pandemic is defined as “occurring over a wide geographic area and affecting an exceptionally high proportion of the population.” The last pandemic reported in the world was the H1N1 flu pandemic in 2009.

On 31 December 2019, a cluster of cases of pneumonia of unknown cause, in the city of Wuhan, Hubei province in China, was reported to the World Health Organization [2].

In January 2020, a previously unknown new virus was identified, subsequently named the 2019 novel coronavirus, and samples obtained from cases and analysis of the virus’ genetics indicated that this was the cause of the outbreak.

This novel coronavirus was named Coronavirus Disease 2019 (COVID-19) by WHO in February 2020. The virus is referred to as SARS-CoV-2 and the associated disease is COVID-19 (Figure 2).

What is Coronavirus?

Coronaviruses are a family of viruses that cause illness such as respiratory diseases or gastrointestinal diseases.

Respiratory diseases can range from the common cold to more severe diseases e.g. Figures 3 and 4

- **Middle East Respiratory Syndrome(MERS-CoV)**

- **Severe Acute Respiratory Syndrome (SARS-CoV).**

A novel coronavirus (nCoV) is a new strain that has not been identified in humans previously [3].

Once scientists determine exactly what coronavirus it is, they give it a name (as in the case of COVID-19, the virus causing it is SARS-CoV-2).

Coronaviruses got their name from the way that they look under a microscope.

The virus consists of a core of genetic material surrounded by an envelope with protein spikes. This gives it the appearance of a crown. The word Corona means “crown” in Latin.

Coronaviruses are zoonotic ,meaning that the viruses are transmitted between animals and humans.

It has been determined that MERS-CoV was transmitted from dromedary camels to humans and SARS-CoV from civet cats to humans.

The source of the SARS-CoV-2 (COVID-19) is yet to be determined, but investigations are ongoing to identify the zoonotic source to the outbreak

Clinical Presentation

Typically Coronaviruses present with respiratory symptoms. Among those who will become infected, some will show no symptoms. Those who do develop symptoms may have a mild to moderate, but self-limiting disease with symptoms similar to the seasonal flu. Symptoms may include:

- Respiratory symptoms
- Fever
- Cough
- Shortness of breath
- Breathing difficulties
- Fatigue
- Sore throat

A minority group of people will present with more severe symptoms and will need to be hospitalised, most often with pneumonia, and in some instances, the illness can include ARDS, sepsis and septic shock. Emergency warning signs where immediate medical attention should be sought include,



Figure 1: History of Coronavirus

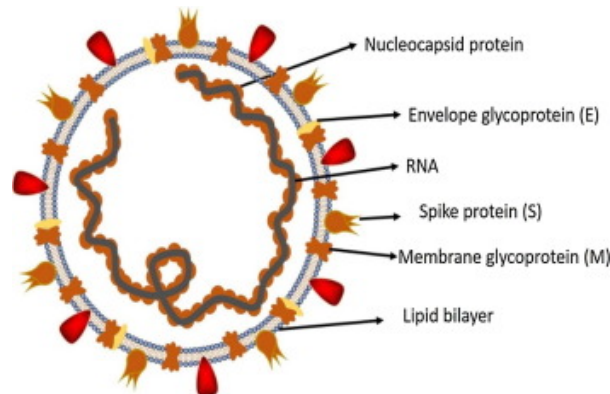


Figure 2: structure of novel coronavirus

- Difficulty breathing or shortness of breath
- Persistent pain or pressure in the chest
- New confusion or inability to arouse
- Bluish lips or face
- High-Risk Po

Older people (people over 70 years of age)
 People with serious chronic illnesses such as,

- Diabetes
- Cardiovascular disease
- Chronic respiratory disease
- Cancer
- Hypertension
- Chronic liver disease

High-Risk Populations

The virus that causes COVID-19 infects people of all ages. However, evidence to date suggests that two groups of people are at a higher risk of getting severe COVID-19 disease:

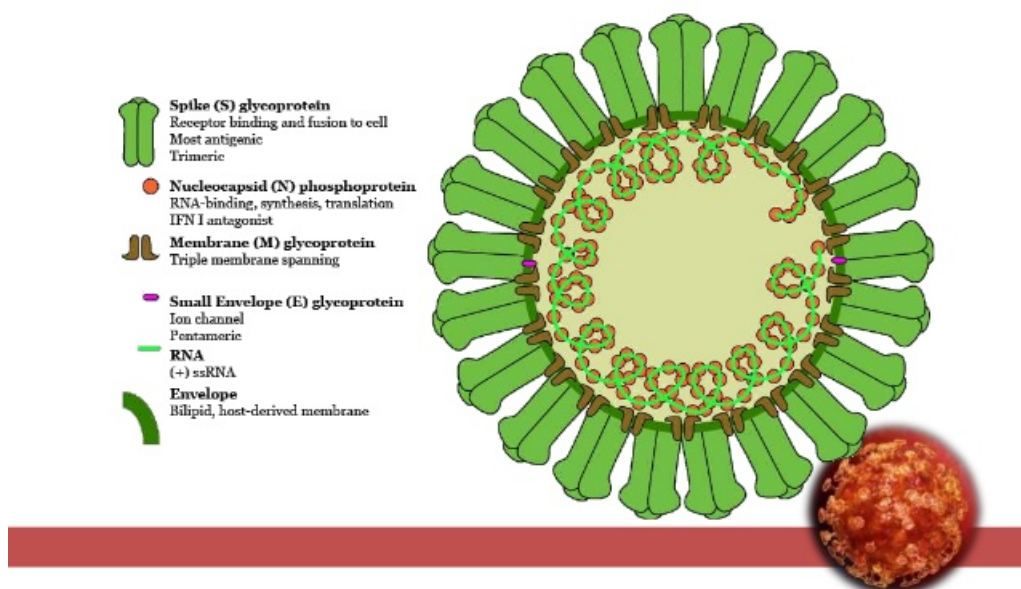


Figure 3: MiddleEast Respiratory Syndrome (MERS-CoV)

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

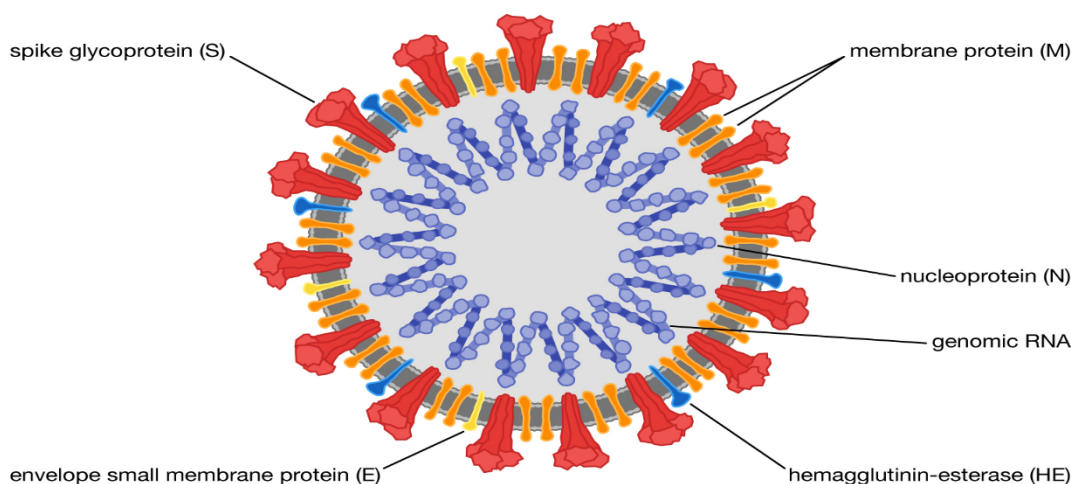


Figure 4: Severe Acute Respiratory Syndrome (SARS-CoV).

The WHO has issued and published advice for these high-risk groups and community support. This is to ensure that these high-risk populations are protected from COVID-19 without being isolated, stigmatized, left in positions of increased vulnerability or unable to have access to basic provisions and social care [4].

WHO advice for high-risk populations

When having visitors at your home, extend “1-meter greetings”, like a wave, nod or bow.

Request that visitors and those who live with you,

wash their hands.

Clean and disinfect surfaces in your home (especially those that people touch a lot) on a regular basis.

Limit shared spaces if someone you live with is not feeling well (especially with possible COVID-19 symptoms).

If you show signs and symptoms of COVID-19 illness, contact your healthcare provider by telephone, before visiting your healthcare facility.

Have an action plan in preparation for an outbreak

of COVID-19 in your community [5].

When you are in public, practice the same preventative guidelines as you would at home [6].

Keep updated on COVID-19 through obtaining information from reliable sources

Transmission of COVID-19

Evidence is still emerging, but current information is indicating that human-to-human transmission is occurring [7].

The routes of transmission of COVID-19 remains unclear at present, but evidence from other coronaviruses and respiratory diseases indicates that the disease may spread through large respiratory droplets and direct or indirect contact with infected secretions.

The incubation period of COVID-19 is currently understood to be between 2 to 14 days.

This means that if a person remains well after 14 days after being in contact with a person with confirmed COVID-19, they are not infected

Preventing Transmission

The WHO suggests the following basic preventative measures to protect against the new coronavirus

Stay up to date with the latest information on the COVID-19 outbreak through WHO updates or your local and national public health authority.

Perform hand hygiene frequently with an alcohol-based hand rub if your hands are not visibly dirty or with soap and water if hands are dirty.

Avoid touching your eyes, nose and mouth [8].

Practice respiratory hygiene by coughing or sneezing into a bent elbow or tissue and then immediately disposing of the tissue.

Wear a medical mask if you have respiratory symptoms and performing hand hygiene after disposing of the mask.

Maintain social distancing (approximately 2 meters) from individuals with respiratory symptoms.

If you have a fever, cough and difficulty breathing seek medical care.

Global Health Security

An international panel of experts undertook a comprehensive assessment and benchmarking of health security and response capabilities across 195 countries. The purpose of the project was to address risks from infectious disease outbreaks that could lead to international epidemics and pandemics and measure response capabilities for each nation. The

hope was that the GHS Index would lead to quantifiable changes in national health security and improve international preparedness [9].

The GHS Index measured indicators across six broad categories:

Prevention

Prevention of the emergence or release of pathogens.

Detection and Reporting

Early detection and reporting for epidemics of potential international concern.

Rapid Response

Rapid response to and mitigation of the spread of an epidemic.

Health System

Sufficient and robust health system to treat the sick and protect health workers.

Compliance with International Norms

Commitments to improving national capacity, financing plans to address gaps, and adhering to global norms.

Risk Environment

Overall risk environment and country vulnerability to biological threats.

Drug development

No medication or vaccine is approved to treat the disease. International research on vaccines and medicines in COVID-19 is underway by government organisations, academic groups, and industry researchers.

In March, the World Health Organisation initiated the "Solidarity Trial" to assess the treatment effects of four existing antiviral compounds with the most promise of efficacy.

The World Health Organization suspended hydroxychloroquine from its global drug trials for COVID-19 treatments on 26 May 2020 due to safety concerns.

It had previously enrolled 3,500 patients from 17 countries in the Solidarity Trial France, Italy and Belgium also banned the use of hydroxychloroquine as a COVID-19 treatment.

There has been a great deal of COVID-19 research, involving accelerated research processes and publishing shortcuts to meet the global demand.

To minimise the harm from misinformation, medical professionals and the public are advised to expect rapid changes to available information, and to be attentive to retractions and other updates.

Vaccine

There is no available vaccine, but various agencies are actively developing vaccine candidates. Previous work on SARS-CoV is being used because both SARS-CoV and SARS-CoV-2 use the ACE2 receptor to enter human cells.

Three vaccination strategies are being investigated. First, researchers aim to build a whole virus vaccine.

The use of such a virus, be it inactive or dead, aims to elicit a prompt immune response of the human body to a new infection with COVID-19. A second strategy, subunit vaccines, aims to create a vaccine that sensitises the immune system to certain subunits of the virus.

In the case of SARS-CoV-2, such research focuses on the S-spike protein that helps the virus intrude the ACE2 enzyme receptor.

A third strategy is that of the nucleic acid vaccines (DNA or RNA vaccines, a novel technique for creating a vaccination).

Experimental vaccines from any of these strategies would have to be tested for safety and efficacy.

On 16 March 2020, the first clinical trial of a vaccine started with four volunteers in Seattle, Washington, United States.

The vaccine contains a harmless genetic code copied from the virus that causes the disease [10].

Antibody-dependent enhancement has been suggested as a potential challenge for vaccine development for SARS-COV-2, but this is controversial.

Medications

At least 29 phase II–IV efficacy trials in COVID-19 were concluded in March 2020, or scheduled to provide results in April from hospitals in China.

There are more than 300 active clinical trials underway as of April 2020.

Seven trials were evaluating already approved treatments, including four studies on hydroxychloroquine or chloroquine.

Repurposed antiviral drugs make up most of the Chinese research, with nine phase III trials on remdesivir across several countries due to report by the end of April. Other candidates in trials include vasodilators, corticosteroids, immune therapies, lipoic acid, bevacizumab, and recombinant angiotensin-converting enzyme 2.

The COVID-19 Clinical Research Coalition has goals to,

Facilitate rapid reviews of clinical trial proposals by ethics committees and national regulatory agencies,

fast-track approvals for the candidate therapeutic compounds, ensure standardised and rapid analysis of emerging efficacy and safety data and facilitate sharing of clinical trial outcomes before publication.

Several existing medications are being evaluated for the treatment of COVID-19, including remdesivir, chloroquine, hydroxychloroquine, lopinavir/ritonavir, and lopinavir/ritonavir combined with interferon beta.

There is tentative evidence for efficacy by remdesivir, as of March 2020. Clinical improvement was observed in patients treated with compassionate-use remdesivir; Remdesivir inhibits SARS-CoV-2 in vitro.

Phase III clinical trials are underway in the U.S., China, and Italy.

In 2020, a trial found that lopinavir/ritonavir was ineffective in the treatment of severe illness. Nitazoxanide has been recommended for further in vivo study after demonstrating low concentration inhibition of SARS-CoV-2.

There are mixed results as of 3 April 2020 as to the effectiveness of hydroxychloroquine as a treatment for COVID-19, with some studies showing little or no improvement, and one study showing an increase in morbidity along with side effects.

The studies of chloroquine and hydroxychloroquine with or without azithromycin have major limitations that have prevented the medical community from embracing these therapies without further study.

Oseltamivir does not inhibit SARS-CoV-2 in vitro and has no known role in COVID-19 treatment.

Cytokine storm

A cytokine storm can be a complication in the later stages of severe COVID-19.

There is preliminary evidence that hydroxychloroquine may be useful in controlling cytokine storms in late-phase severe forms of the disease.

Tocilizumab has been included in treatment guidelines by China's National Health Commission after a small study was completed.

It is undergoing a phase 2 non-randomised trial at the national level in Italy after showing positive results in people with severe disease. [Combined with a serum ferritin blood test to identify a cytokine storm (also called cytokine storm syndrome, not to be confused with cytokine release syndrome), it is meant to counter such developments, which are thought to be the cause of death in some affected people.

The interleukin-6 receptor antagonist was approved

by the FDA to undergo a phase III clinical trial assessing the its effectiveness on COVID-19 based on retrospective case studies for the treatment of steroid-refractory cytokine release syndrome induced by a different cause, CAR T cell therapy, in 2017.

To date, there is no randomised, controlled evidence that tocilizumab is an efficacious treatment for CRS. Prophylactic tocilizumab has been shown to increase serum IL-6 levels by saturating the IL-6R, driving IL-6 across the blood-brain barrier, and exacerbating neurotoxicity while having no effect on the incidence of CRS.

Lenzilumab, an anti-GM-CSF monoclonal antibody, is protective in murine models for CAR T cell-induced CRS and neurotoxicity and is a viable therapeutic option due to the observed increase of pathogenic GM-CSF secreting T-cells in hospitalised patients with COVID-19.

The Feinstein Institute of Northwell Health announced in March a study on "a human antibody that may prevent the activity" of IL-6.

Passive antibodies

Transferring purified and concentrated antibodies produced by the immune systems of those who have recovered from COVID-19 to people who need them is being investigated as a non-vaccine method of passive immunisation.

This strategy was tried for SARS with inconclusive results.

Viral neutralisation is the anticipated mechanism of action by which passive antibody therapy can mediate defence against SARS-CoV-2. Other mechanisms, however, 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.

Production of convalescent serum, which consists of the liquid portion of the blood from recovered patients and contains antibodies specific to this virus, could be increased for quicker deployment.

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Conflict of Interest

Authors declared no conflict of interest.

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