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CORONA VIRUS – A REVIEW

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ABSTRACT

Coronavirus is a larger family of viruses that cause illnesses such as the common cold, severe acute respiratory syndrome (SARS), and the Middle East respiratory syndrome (MERS). A new outbreak of the coronavirus erupted in 2019 in China. Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus.Some other names attributed to the coronavirus are severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the coronavirus disease 2019 (COVID-19). Coronavirus affects both animals and humans. There can be cases where the virus affects animals and turns into a new virus that affects humans. These are more lethal forms of coronavirus since they can lead to pneumonia, which can be life-threatening. The name "coronavirus" comes from the crown-like projections on their surfaces. "Corona" in Latin means "halo" or "crown."

INTRODUCTION

In 2019, the Centers for Disease Control and Prevention (CDC) started monitoring the outbreak of a new coronavirus, SARS-CoV-2, which causes COVID-19. Authorities first identified the virus in Wuhan, China. The corona virus COVID-19 is affecting 213 countries and territories around the world and 2 international conveyances. Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness. The three most common illnesses by the virus recorded are: SARS (severe acute respiratory syndrome) – It's a fatal respiratory illness discovered in China in 2002. There haven't been any new cases reported under this virus since 2002.

- MERS (Middle East respiratory syndrome) – This severe respiratory illness was first reported in Saudi Arabia in 2012. From there, it spread to 27 countries including the USA, where two cases were reported. All cases were discovered to have their source in the Arabian Peninsula. COVID-19 (coronavirus disease 2019) – Erupting in Wuhan city in 2019, the source is travel from the Hubei Province. Since then, the disease has spread to several countries around the world, with some cases reported in the USA. All updates with regards to the disease are being monitored by the Centers for Disease Control (CDC) and the World Health Organization (WHO).The best way to prevent and slow down transmission is be well informed about the COVID-19 virus, the disease it causes and how it spreads. Protect yourself and others from infection by washing your hands or using an alcohol based rub frequently and not touching

- your face. The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes, so it's important that you also practice respiratory etiquette (for example, by coughing into a flexed elbow).At this time, there are no specific vaccines or treatments for COVID-19. However, there are many ongoing clinical trials evaluating potential treatments. WHO will continue to provide updated information as soon as clinical findings become available

Incubation period for COVID-19: It appears that symptoms are showing up in people within 14 days of exposure to the virus.

Types: Coronaviruses belong to the subfamily Coronavirinae in the family coronaviridae. Different types of coronavirus vary, in terms of the severity of disease that they cause and how far they spread. Doctors currently recognize seven types of coronavirus that can infect humans.

Common types include:

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

Rarer strains that cause more severe illnesses include MERS-CoV, which causes the disease MERS, and SARS-CoV, the virus responsible for SARS. In 2019, a new strain, called SARS-CoV-2, started circulating, causing the disease COVID-19.

STRUCTURE OF CORONA VIRUS: Spherical or pleomorphic enveloped particles containing single-stranded (positive-sense) RNA associated with a nucleoprotein within a capsid comprised of matrix protein. The envelope bears club-shaped glycoprotein projections. Coronaviruses belong to the family Coronaviridae in the order Nidovirales . They can be classified into four genera: Alphacoronavirus, Betacoronavirus, Ga mmacoronavirus, and Deltacoronavirus . Among them, alpha- and betacoronaviruses infect mammals, gammacoronaviruses infect avian species, and deltacoronaviruses infect both mammalian and avian species. Representative alphacoronaviruses include human coronavirus NL63 (HCoV-NL63), porcine transmissible gastroenteritis coronavirus (TGEV), PEDV, and porcine respiratory coronavirus (PRCV). Representative betacoronaviruses include SARS-CoV, MERS-CoV, bat coronavirus HKU4, mouse hepatitis coronavirus (MHV), bovine coronavirus (BCoV), and human coronavirus OC43. Representative gamma- and deltacoronaviruses include avian infectious bronchitis coronavirus (IBV) and porcine deltacoronavirus (PdCV), respectively. Coronaviruses are large, enveloped, positive-stranded RNA viruses. They have the largest genome among all RNA viruses, typically ranging from 27 to 32 kb. The genome is packed inside a helical capsid formed by the nucleocapsid protein (N) and further surrounded by an envelope. Associated with the viral envelope are at least three structural proteins: The membrane protein (M) and the envelope protein (E) are involved in virus assembly, whereas the spike protein (S) mediates virus entry into host cells. Some coronaviruses also encode an envelope-associated hemagglutinin-esterase protein (HE). Among these structural proteins, the spike forms large protrusions from the virus surface, giving coronaviruses the appearance of having crowns (hence their name; corona in Latin means crown) (**Figures 1b** and **2a**). In addition to mediating virus entry, the spike is a critical determinant of viral host range and tissue tropism and a major inducer of host immune responses.

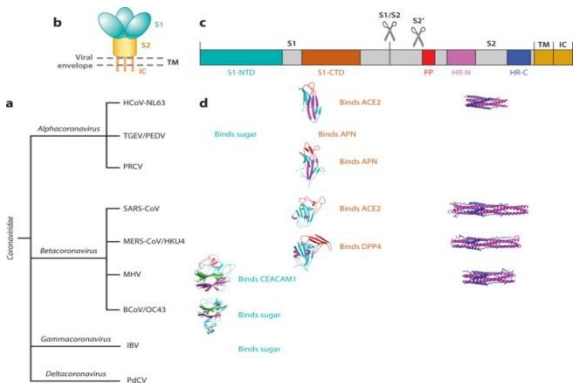

Figure 1

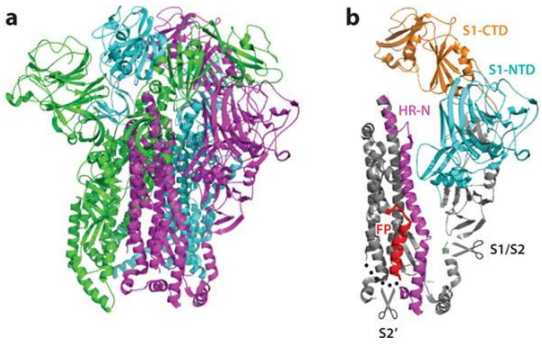

Figure 2

The coronavirus spike contains three segments: a large ectodomain, a single-pass transmembrane anchor, and a short intracellular tail (Figure 1*b*,*c*). The ectodomain consists of a receptor-binding subunit S1 and a membrane-fusion subunit S2. Electron microscopy studies revealed that the spike is a clove-shaped trimer with three S1 heads and a trimeric S2 stalk (15–18) (Figures 1*b* and 2*a*). During virus entry, S1 binds to a receptor on the host cell surface for viral attachment, and S2 fuses the host and viral membranes, allowing viral genomes to enter host cells. Receptor binding and membrane fusion are the initial and critical steps in the coronavirus infection cycle; they also serve as primary targets for human inventions.

SYMPTOMS: On average it takes 5–6 days from when someone is infected with the virus for symptoms to show, however it can take up to 14 days. Seek immediate medical attention if you have serious symptoms. Always call before visiting your doctor or health facility. People with mild symptoms who are otherwise healthy should manage their symptoms at home.

Most common symptoms:

- Fever.
- Dry cough.
- Tiredness.

Less common symptoms:

- Aches and pains.
- Sore throat.
- Diarrhoea.
- Conjunctivitis.
- Headache.
- Loss of taste or smell.
- A rash on skin, or discoloration of fingers or toes.

Serious symptoms:

- Difficulty breathing or shortness of breath.
- Chest pain or pressure.
- Loss of speech or movement.

DIAGNOSIS:

Diagnosis may be difficult with only a physical exam because mild cases of COVID-19 may appear similar to the flu or a bad cold. A doctor can identify the virus responsible in a sample of fluid from a person's body, such as a sample of blood or mucus from the nose. A laboratory test can confirm the diagnosis. . Laboratory diagnosis may be made on the basis of antibody titers in paired sera. The virus is difficult to isolate. Nucleic acid hybridization tests (including PCR) are now being introduced.

PREVENTION:

To prevent infection and to slow transmission of COVID-19, do the following:

- Wash your hands regularly with soap and water, or clean them with alcohol-based hand rub.
- Maintain at least 1 metre distance between you and people coughing or sneezing.
- Avoid touching your face.
- Cover your mouth and nose when coughing or sneezing.
- Stay home if you feel unwell.
- Refrain from smoking and other activities that weaken the lungs.
- Practice physical distancing by avoiding unnecessary travel and staying away from large groups of people.

TREATMENT: There is currently no cure for the cold-like illnesses caused by coronaviruses. Treatments include self-care and over-the-counter medications. Taking the following steps may help:

- Resting and avoiding overexertion
- Drinking plenty of water
- Aoiding smoking and smoky areas
- Taking acetaminophen (Tylenol) to reduce pain and a fever
- Using a clean humidifier or cool mist vaporizer

Hospitals and research labs all over the world are testing many different therapies on coronavirus-positive patients in an effort to find a potential COVID-19 treatment. Below we highlight a few medications and treatments that have been making a buzz in the science community.

Remdesivir

The broad-spectrum antiviral agent remdesivir (GS-5734; Gilead Sciences, Inc) is a nucleotide analogprodrug. On May 1, 2020, The US FDA issued EUA of remdesivir to allow emergency use of the agent for severe COVID-19 (confirmed or suspected) in hospitalized adults and children. A phase 1b trial of an inhaled nebulized version was initiated in late June 2020 to determine if remdesivir can be used on an outpatient basis and at earlier stages of disease. It was studied in clinical trials for Ebola virus infections but showed limited benefit. Remdesivir has been shown to inhibit replication of other human coronaviruses associated with high morbidity in tissue cultures, including severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003 and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012. Efficacy in animal models has been demonstrated for SARS-CoV and MERS-CoV.

Dexamethasone

Dexamethasone is a common corticosteroid (steroid) medication that has been used for many years to treat various health conditions, such as autoimmune conditions and allergic reactions. RECOVERY, a randomized clinical trial in the UK, is studying many medications, including dexamethasone, to see if any are effective against COVID-19.

Hydroxychloroquine and chloroquine

Hydroxychloroquine and chloroquine are two medications that have been used for many decades to treat malaria and autoimmune conditions like rheumatoid arthritis and lupus. A few small studies suggest that they may also be helpful for treating hospitalized patients with mild cases of COVID-19, while many other studies showed that hydroxychloroquine did not make a difference. More robust studies are needed to confirm whether these medications actually work.

Azithromycin

Azithromycin (informally known as a Z-pak) is an antibiotic commonly used to treat bacterial infections such as bronchitis and pneumonia. It has been shown to have some *in vitro* activity against viruses like influenza A and Zika, but did not work against the coronavirus that causes MERS. One research group looked at azithromycin in combination with hydroxychloroquine for COVID-19. They reported that 93% of patients cleared the virus after 8 days, but there was no control group so we don't know if people would have cleared the virus on their own without the medications. There are concerns about potentially serious side effects when using azithromycin and hydroxychloroquine together.

Convalescent plasma

On March 24, 2020, the FDA issued an Emergency Investigational New Drug (eIND) application for the use of convalescent plasma to treat people with COVID-19. Plasma is the liquid part of blood that carries blood cells. Convalescent plasma is collected from people who have recovered from COVID-19. It is then transfused into someone with an active coronavirus infection. It is thought that antibodies found in the convalescent plasma can help fight the coronavirus infection. The first convalescent plasma transfusion in the U.S. for COVID-19 was recently done in Texas. A physician can request convalescent plasma on an individual basis by contacting their local blood center, but it's not widely available since centers have just recently begun collecting it.

Tocilizumab (Actemra)

Tocilizumab is a disease-modifying anti-rheumatic drug (DMARD) approved for rheumatoid arthritis and juvenile idiopathic arthritis. (Both are inflammatory diseases.) It works by blocking interleukin-6 (IL-6), a protein involved in our natural immune responses. IL-6 normally signals other cells to activate the immune system, but too much activation can cause issues. One possible serious issue with an overactive immune system is a cytokine storm, a potentially fatal problem in which the immune system goes haywire and inflammation gets out of control. With COVID-19, people can be at risk of cytokine storms as their bodies continue to ramp up their immune system to fight off the infection. By blocking IL-6, tocilizumab helps to calm down the immune system and is believed to also help with managing cytokine storms. A study from France reported that people who got tocilizumab were less likely to require ventilation or die. Another study from Italy found that those who got tocilizumab had a lower death rate, though about the same percentage of patients from both groups needed ventilators. On the other hand, tocilizumab did not help COVID-19 patients with early-stage pneumonia.

Kaletra (lopinavir/ritonavir)

Kaletra is an HIV medication containing a combination of two antivirals called lopinavir and ritonavir. *In vitro* and clinical studies looking at patients who had previously received these antiviral agents suggest that they may have some activity against SARS and MERS (infections caused by other coronaviruses). Data for using Kaletra in COVID-19 is limited. In one randomized study of 199 people hospitalized with COVID-19, there was no difference between using Kaletra and not using it in terms of how long it took for patients to improve. Another small study of 127 people with mild COVID-19 symptoms looked at Kaleta alone compared to Kaletra in combination with interferon beta-1b and ribavirin. They found that the group who got all three medications improved sooner and cleared the virus faster (7 days) than those who only got Kaletra (12 days).

Tamiflu (oseltamivir)

Tamiflu is an antiviral medication used for influenza (flu). Results from a hospital in Wuhan, China were not promising. Of 138 hospitalized patients, 124 got Tamiflu along with other medications. By the end of the study, 85 patients (62%) were still hospitalized and 6 had died. Nonetheless, several clinical trials are currently looking at Tamiflu in combination with other medications for coronavirus.

Avigan (favipiravir) and other antiviral medications

Favipiravir (also known as Avigan) is an antiviral medication approved in Japan and China for the flu. *In vitro* studies have shown that high doses of favipiravir were able to prevent human cells from being infected with SARS-CoV-2. Two studies in China looked at how favipiravir worked in comparison to other antivirals. In a study of 240 patients in China with mild COVID-19 symptoms, 71% of patients given favipiravir recovered after 7 days compared to 56% who were given umifenovir (Arbidol). Another small study in China looked at 80 patients with mild COVID-19 symptoms and saw that that favipiravir helped to clear the virus faster than Kaletra (4 days vs. 11 days, respectively). The patients who took favipiravir also showed greater improvements in their lungs based on chest images. The first U.S. clinical trials for favipiravir were recently approved to start in Boston. Other antivirals being tested for COVID-19 include umifenovir and galidesivir:

- Umifenovir (Arbidol) is a flu medication that is used outside the U.S. As mentioned above, it was not as good as favipiravir in helping patients recover in a study from China. Another study of 81 patients looked at how long it took from when patients first had symptoms to when they tested negative for the coronavirus, and it found that there was no difference

between people who got umifenovir and those who did not. However, it seems to be better than Kaletra at helping patients with COVID-19 clear the virus. In a small study of 50 people, the virus was not detected in any patients who had received umifenovir after 14 days. The virus was still present in almost half of the patients who got Kaletra.

- Galidesivir is a new drug that is currently being developed for a variety of viral infections; it has not yet been approved for human use. Clinical trials for galidesivir are starting in Brazil.

Colcrys (colchicine)

Colchicine is a medication used for gout. It works in many different ways, including activating anti-inflammatory processes and interfering with cells involved in inflammation. Researchers think that colchicine could work similarly to tocilizumab (Actemra) in COVID-19 patients in that it might be helpful if the immune system becomes too activated and a cytokine storm occurs. A large clinical trial is currently seeing if colchicine, when given soon after a COVID-19 diagnosis, can lower the chances of hospitalization and death.

11) Ivermectin

Ivermectin is an oral medication used to treat infections caused by parasites. It is also available as a lotion or cream to treat lice and rosacea. A recent *in vitro* study found that ivermectin can stop SARS-CoV-2 from replicating. A lot more research is needed to see if the doses studied would be safe and effective against the virus in humans.

What are FDA-approved treatments for coronavirus (COVID-19)?

There are currently no FDA-approved treatments for coronavirus. The FDA recently created a new emergency program, Coronavirus Treatment Acceleration Program (CTAP), aimed at speeding up research for the development of COVID-19 treatments.

For now, the treatment for patients with mild symptoms is to self-isolate at home. Patients who are hospitalized receive supportive care (such as oxygen), enroll in clinical trials, and are given medications off-label based on hospital guidelines and their doctors' clinical judgement.

VACCINE FOR COVID-19

There is no cure or vaccine for COVID-19 at this time. More studies are needed to confirm if any of the potential treatments listed above will work for COVID-19. Research on COVID-19 is rapidly evolving. Samples of the COVID-19 virus are arriving at laboratories in the United States and around the world and scientists are studying the virus to find ways to treat it, develop a vaccine, and ultimately stop it. On July 27, 2020, NIAID announced that a Phase 3 clinical trial designed to evaluate if an investigational vaccine can prevent symptomatic coronavirus disease 2019 (COVID-19) in adults has begun. The vaccine, known as mRNA-1273, was co-developed by the Cambridge, Massachusetts-based biotechnology company Moderna, Inc., and the National Institute of Allergy and Infectious Diseases. The trial, which will be conducted at U.S. clinical research sites, is expected to enroll approximately 30,000 adult volunteers who do not have COVID-19. NIAID scientists developed the stabilized SARS-CoV-2 "spike" immunogen* (S-2P). The spike protein on the surface of SARS-CoV-2 facilitates entry into a cell. Moderna's mRNA-1273 uses the mRNA (messenger RNA) delivery platform to encode for an S-2P immunogen. The investigational vaccine directs the body's cells to express the spike protein to elicit a broad immune response. A Phase 1 clinical trial found the candidate vaccine to be safe, generally well-tolerated and able to induce antibodies with high levels of virus-neutralizing activity. Moderna initiated Phase 2 testing of the vaccine in May 2020.

*An immunogen is a specific type of antigen that is able to elicit an immune response.

Vaccines are the best way to stop the spread of COVID-19 and other infectious diseases, but traditionally they take years to develop and test. It took 20 months after the SARS outbreak to develop a vaccine, and by then the virus had died out. It took just 6 months to develop a Zika vaccine in 2015. Scientists are hopeful that this time they can build on previous knowledge to develop a vaccine rapidly.

CONCLUSION:

The World Health Organization declared the novel coronavirus outbreak "a public health emergency of international concern" on January 30. On March 11, 2020 after sustained spread of the disease outside of China, the World Health Organization declared the COVID-19 epidemic a pandemic. Public health measures like ones implemented in China and now around the world, will hopefully blunt the spread of the virus while treatments and a vaccine are developed to stop it. The novel coronavirus infections were at first associated with travel from Wuhan, but the virus has now established itself in 177 countries and territories around the world in a rapidly expanding pandemic. Health officials in the United States and around the world are working to contain the spread of the virus through public health measures such as social distancing, contact tracing, testing, quarantines and travel restrictions. Scientists are working to find medications to treat the disease and to develop a vaccine.

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