

A REVIEW - COVID-19 (A NOVEL CORONA VIRUS)

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Abstract: An acute respiratory disease, caused by a novel corona virus (SARS-CoV-2, previously known as 2019-nCoV), the corona virus disease 2019 (COVID-19) has spread throughout China and received worldwide attention. On 30 January 2020, World Health Organization (WHO) officially declared the COVID-19 epidemic as a public health emergency of international concern. The emergence of SARS-CoV-2, since the severe acute respiratory syndrome corona virus (SARS-CoV) in 2002 and Middle East respiratory syndrome corona virus (MERS-CoV) in 2012, marked the third introduction of a highly pathogenic and large-scale epidemic corona virus into the human population in the twenty-first century. Several independent research groups have identified that SARS-CoV-2 belongs to β -corona virus, with highly identical genome to bat corona virus, pointing to bat as the natural host. The novel corona virus uses the same receptor, angiotensin-converting enzyme 2 (ACE2) as that for SARS-CoV, and mainly spreads through the respiratory tract. Importantly, increasingly evidence showed sustained human-to-human transmission, along with many exported cases across the globe. The clinical symptoms of COVID-19 patients include fever, cough, fatigue and a small population of patients appeared gastrointestinal infection symptoms.

Keywords: COVID-19, SARS-CoV, (ACE2) Angiotensin-converting enzyme 2

Background:

In December 2019, many pneumonia cases that were clustered in Wuhan city were reported and searches for the source have shown Huanan Seafood Market as the origin. The first case of the COVID-19 epidemic was discovered with unexplained pneumonia on December 12, 2019, and 27 viral pneumonia cases with seven being severe, were officially announced on December 31, 2019.^[1,2] Etiologic investigations have been performed in patients who applied to the hospital due to similar viral pneumonia findings. On January 22, 2020, novel CoV has been declared to be originated from wild bats and belonged to Group 2 of beta-coronavirus that contains Severe Acute Respiratory Syndrome Associated Coronavirus (SARS-CoV). Although COVID-19 and SARS-CoV belong to the same beta coronavirus subgroup, similarity at genome level is only 70%, and the novel group has been found to show genetic differences from SARS-CoV.^[3]

Introduction:

Coronavirus disease 2019 (COVID-19) is a respiratory illness that can spread from person to person. The virus that causes COVID-19 is a novel coronavirus that was first identified during an investigation into an outbreak in Wuhan, China. [4]

Coronaviruses:

Coronaviruses are a group of related viruses that cause diseases in mammals and birds. In humans, coronaviruses cause respiratory tract infections that can be mild, such as some cases of the common cold (among other possible causes, predominantly rhinoviruses), and others that can be lethal, such as SARS, MERS, and COVID-19. Symptoms in other species vary: in chickens, they cause an upper respiratory tract disease, while in cows and pigs they cause diarrhea. There are yet to be vaccines or antiviral drugs to prevent or treat human coronavirus infections.^[3] Coronaviruses constitute the subfamily Orthocoronavirinae, in the family Coronaviridae, order Nidovirales, and realm Riboviria. They are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry. The genome size of coronaviruses ranges from approximately 27 to 34 kilobases, the largest among known RNA viruses. The name coronavirus is derived from the Latin corona, meaning "crown" or "halo", which refers to the characteristic appearance reminiscent of a crown or a solar corona around the virions (virus particles) when viewed under two-dimensional transmission electron microscopy, due to the surface being covered in club-shaped protein spikes.^[6]

Discovery:

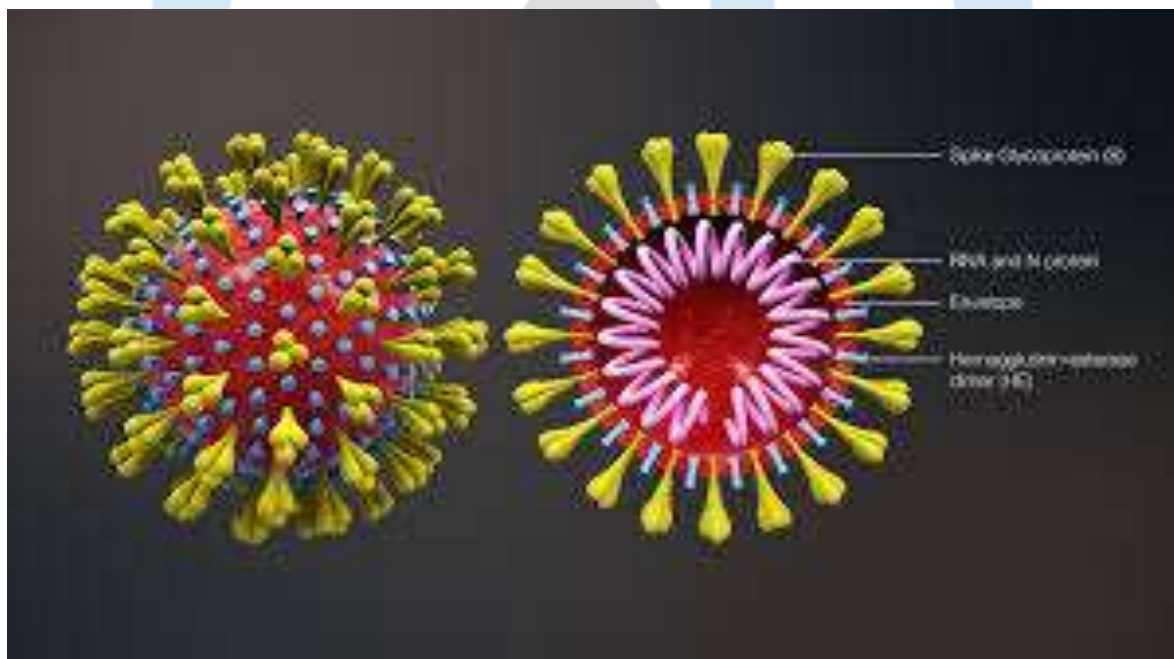
Human coronaviruses were first discovered in the late 1960s. The earliest ones discovered were an infectious bronchitis virus in chickens and two in human patients with the common cold (later named human coronavirus 229E and human coronavirus OC43). Other members of this family have since been identified, including SARS-CoV in 2003, HCoV NL63 in 2004, HKU1 in 2005, MERS-CoV in 2012, and SARS-CoV-2 (formerly known as 2019-nCoV) in 2019. Most of these have involved serious respiratory tract infections.^[7]

In December 2019, a pneumonia outbreak was reported in Wuhan, China. On 31 December 2019, the outbreak was traced to a novel strain of coronavirus, which was given the interim name 2019-nCoV by the World Health Organization (WHO), later renamed SARS-CoV-2 by the International Committee on Taxonomy of Viruses. Some researchers have suggested that the Huanan Seafood Wholesale Market may not be the original source of viral transmission to humans. As of 30 March 2020 (Global status), there have been at least 34,822 confirmed deaths and more than 5,47,452 confirmed cases in the coronavirus pneumonia pandemic and recovered cases 1,51,789. The Wuhan strain has been identified as a new strain of Betacoronavirus from group 2B with

approximately 70% genetic similarity to the SARS-CoV. The virus has a 96% similarity to a bat coronavirus, so it is widely suspected to originate from bats as well. The pandemic has resulted in travel restrictions and nationwide lockdowns in several countries.[6]

Causes of Diseases:

Coronaviruses primarily infect the upper respiratory and gastrointestinal tract of mammals and birds. They also cause a range of diseases in farm animals and domesticated pets, some of which can be serious and are a threat to the farming industry. In chickens, the infectious bronchitis virus (IBV), a coronavirus, targets not only the respiratory tract but also the urogenital tract. The virus can spread to different organs throughout the chicken. Economically significant coronaviruses of farm animals include porcine coronavirus (transmissible gastroenteritis coronavirus, TGE) and bovine coronavirus, which both result in diarrhea in young animals. Feline coronavirus: two forms, feline enteric coronavirus is a pathogen of minor clinical significance, but spontaneous mutation of this virus can result in feline infectious peritonitis (FIP), a disease associated with high mortality. Similarly, there are two types of coronavirus that infect ferrets: Ferret enteric coronavirus causes a gastrointestinal syndrome known as epizootic catarrhal enteritis (ECE), and a more lethal systemic version of the virus (like FIP in cats) known as ferret systemic coronavirus (FSC). There are two types of canine coronavirus (CCoV), one that causes mild gastrointestinal disease and one that has been found to cause respiratory disease. Mouse hepatitis virus (MHV) is a coronavirus that causes an epidemic murine illness with high mortality, especially among colonies of laboratory mice. Sialodacryoadenitis virus (SDAV) is highly infectious coronavirus of laboratory rats, which can be transmitted between individuals by direct contact and indirectly by aerosol. Acute infections have high morbidity and tropism for the salivary, lachrymal and Harderian glands. [8] A HKU2-related bat coronavirus called swine acute diarrhea syndrome coronavirus (SADS-CoV) causes diarrhea in pigs. Prior to the discovery of SARS-CoV, MHV had been the best-studied coronavirus both in vivo and in vitro as well as at the molecular level. Some strains of MHV cause a progressive demyelinating encephalitis in mice which has been used as a murine model for multiple sclerosis. Significant research efforts have been focused on elucidating the viral pathogenesis of these animal coronaviruses, especially by virologists interested in veterinary and zoonotic diseases.[9]



Structure: Cross-sectional model of a coronavirus

Human Coronaviruses

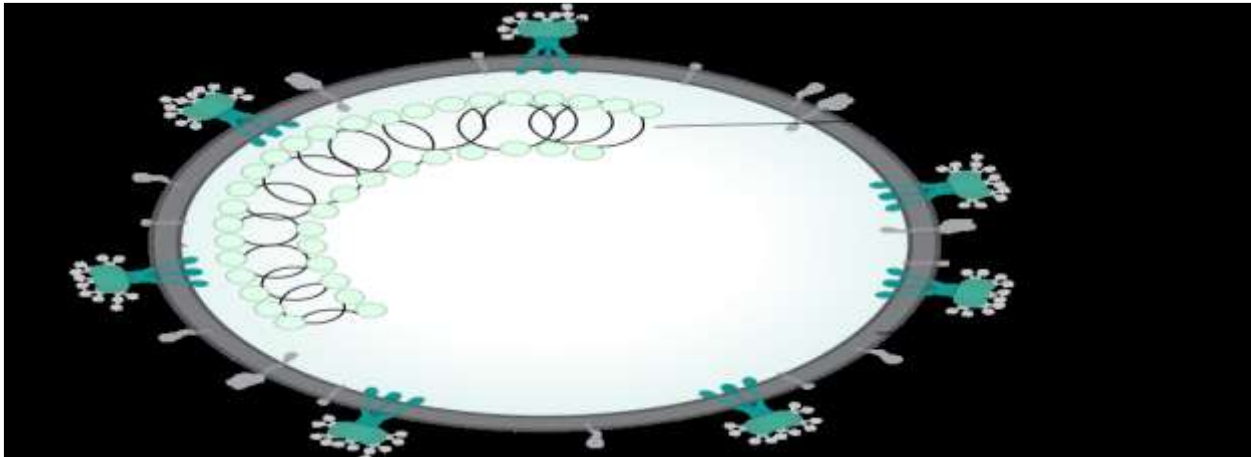
Coronaviruses vary significantly in risk factor. Some can kill more than 30% of those infected (such as MERS-CoV), and some are relatively harmless, such as the common cold. Coronaviruses cause colds with major symptoms, such as fever, and sore throat from swollen adenoids, occurring primarily in the winter and early spring seasons. Coronaviruses can cause pneumonia (either direct viral pneumonia or a secondary bacterial pneumonia) and bronchitis (either direct viral bronchitis or a secondary bacterial bronchitis). The much publicized human coronavirus discovered in 2003, SARS-CoV, which causes severe acute respiratory syndrome (SARS), has a unique pathogenesis because it causes both upper and lower respiratory tract infections.[10]

Seven strains of human coronaviruses are known, of which four produce the generally mild symptoms of the common cold:

1. Human coronavirus OC43 (HCoV-OC43)
2. Human coronavirus HKU1
3. Human coronavirus NL63 (HCoV-NL63, New Haven coronavirus)
4. Human coronavirus 229E (HCoV-229E)

Three, symptoms that are potentially severe:

1. Middle East respiratory syndrome-related coronavirus (MERS-CoV), previously known as novel coronavirus 2012 and HCoV-EMC
 2. Severe acute respiratory syndrome coronavirus (SARS-CoV or "SARS-classic")
 3. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), previously known as 2019-nCoV or "novel coronavirus2019"
- The coronaviruses HCoV-229E, -NL63, -OC43, and -HKU1 continually circulate in the human population and cause respiratory infections in adults and children world-wide. [11]



Structure: Illustration of SARSr-CoV virion

Symptoms of Coronavirus:

Coronavirus can make people sick, usually with a mild to moderate upper respiratory tract illness, similar to a common cold. Some of the symptoms are

- A general feeling of being unwell
- Runny nose
- Sore throat
- Headache
- Cough
- Fever

Cold- or flu-like symptoms usually set in from 2–4 days after a coronavirus infection and are typically mild. However, symptoms vary from person-to-person, and some forms of the virus can be fatal. Symptoms may include: sneezing runny nose fatigue cough fever sore throat exacerbated asthma. Symptoms vary from person-to-person with COVID-19. It may produce few or no symptoms. However, it can also lead to severe illness and may be fatal. Common symptoms include: fever breathlessness cough potential loss of taste or smell. It may take 2–14 days for a person to notice symptoms after infection. [12]

Coronavirus and Pregnancy:

In pregnant women, the severe versions of SARS and MERS coronaviruses were found to be severe. According to reports, women who suffered from severe versions of coronaviruses had still birth. The National Institutes of Health (NIH) suggest that several groups of people have the highest risk of developing complications due to COVID19. These groups include: young children people aged 65 years or older women who are pregnant.

Preventive Measures:

- Wash your hands thoroughly with soap
- Avoid touching your eyes, nose, or mouth with unclean hands
- Avoid close contact with people who are sick
- Avoid public gatherings

Although there is no vaccine available to prevent infection with the new coronavirus, you can take steps to reduce your risk of infection.

WHO and CDC recommend following these precautions for avoiding COVID-19:

- Avoid large events and mass gatherings.
- Avoid close contact (about 6 feet) with anyone who is sick or has symptoms.
- Keep distance between yourself and others if COVID-19 is spreading in your community, especially if you have a higher risk of serious illness.
- Wash your hands often with soap and water for at least 20 seconds, or use an alcohol-based hand sanitizer that contains atleast 60% alcohol.
- Cover your mouth and nose with your elbow or a tissue when you cough or sneeze. Throw away the used tissue.
- Avoid touching your eyes, nose and mouth if your hands aren't clean.

- Avoid sharing dishes, glasses, bedding and other household items if you're sick.
- Clean and disinfect surfaces you often touch on a daily basis.
- Stay home from work, school and public areas if you're sick, unless you're going to get medical care. Avoid taking public transportation if you're sick.

CDC doesn't recommend that healthy people wear a face mask to protect themselves from respiratory illnesses, including COVID-19.

WHO also recommends that you:

- Avoid eating raw or undercooked meat or animal organs.
- Avoid contact with live animals and surfaces they may have touched if you're visiting live markets in areas that have recently had new coronavirus cases.
- If you have a chronic medical condition and may have a higher risk of serious illness, check with your doctor about other ways to protect yourself. [13]

Complications:

Based on the current information, most patients had a good prognosis, while a few patients were in critical condition, especially the elderly and those with chronic underlying diseases. As of 1 March 2020, a total of 79,968 confirmed cases, including 14,475 (18.1%) with severe illness, and 2873 deaths (3.5%) in mainland China had been reported by WHO [7]. Complications included acute respiratory distress syndrome (ARDS), arrhythmia, shock, acute kidney injury, acute cardiac injury, liver dysfunction and secondary infection. The poor clinical outcome was related to disease severity. The disease tends to progress faster in elderly people, with the median number of days from the occurrence of the first symptoms to death shorter among people aged 65 years or more. Similar to H7N9 patients, the elderly male with comorbidities and ARDS showed a higher death risk. Additionally, more than 100 children were infected, with the youngest being 30 h after birth. Neonates and the elderly need more attention and care due to their immature or weak immune system. [14]

Treatment Of Covid-19:





















Current therapies

Given the lack of effective antiviral therapy against COVID-19, current treatments mainly focused on symptomatic and respiratory support according to the Diagnosis and Treatment of Pneumonia Caused by COVID-19 (updated to version 6) issued by National Health Commission of the People's Republic of China. Nearly all patients accepted oxygen therapy, and WHO recommended extracorporeal membrane oxygenation (ECMO) to patients with refractory hypoxemia. Rescue treatment with convalescent plasma and immunoglobulin G are delivered to some critical cases according to their conditions.

Antiviral treatments

Based on the experience of fighting the epidemic SARSCoV and MERS-CoV previously, we may learn some lessons for some treatment strategies against coronavirus. Antiviral drugs and systemic corticosteroid treatment commonly used in clinical practice previously, including neuraminidase inhibitors (oseltamivir, peramivir, zanamivir, etc), ganciclovir, acyclovir, and ribavirin, as well as methylprednisolone for influenza virus, are invalid for COVID-19 and not recommended. Remdesivir (GS-5734) is a 1'-cyanosubstituted adenosine nucleotide analog prodrug and shows broad spectrum antiviral activity against several RNA viruses. Based on the data collected from in vitro cell line and mouse model, remdesivir could interfere with the NSP12 polymerase even in the setting of intact ExoN proofreading activity. Remdesivir has been reported to treat the first US case of COVID-19 successfully. Chloroquine is a repurposed drug with great potential to treat COVID-19. Chloroquine has been used to treat malaria for many years, with a mechanism that is not well understood against some viral infections. Several possible mechanisms are investigated: Chloroquine can inhibit pH-dependent steps of the replication of several viruses, with a potent effect on SARS-CoV infection and spread. Moreover, chloroquine has immunomodulatory effects, suppressing the production/release of TNF- α and IL-6. It also works as a novel class of autophagy inhibitor, which may interfere with viral infection and replication. Several studies have found that chloroquine interfered with the glycosylation of cellular receptors of SARS-CoV and functioned at both entry and at post-entry stages of the COVID-19 infection in Vero E6 cells. A combination of remdesivir and chloroquine was proven to effectively inhibit the recently emerged SARS-CoV-2 in vitro. Scientists previously confirmed that the protease inhibitors lopinavir and ritonavir, used to treat infection with human immunodeficiency virus (HIV), could improve the outcome of MERS-CoV and SARSCoV patients. It has reported that β -coronavirus viral loads of a COVID-19 patient in Korea significantly decreased after lopinavir/ritonavir (Kaletra®, AbbVie, North Chicago, IL, USA) treatment. Additionally, clinicians combined Chinese and Western medicine treatment including lopinavir/ritonavir (Kaletra®), arbidol, and Shufeng Jied Capsule (SFJDC, a traditional Chinese medicine) and gained significant improvement in pneumonia associated symptoms in Shanghai Public Health Clinical Center, China. The other antiviral drugs include nitazoxanide, favipiravir. [13]

Current activities by pharma:

 Organization	 Type	 Target	 Phase
 GILEAD	Treatment	Remdesivir	III
 SANOFI	Treatment + Vaccine	Plaquenil®	Preclinical
 BIONTECH	Treatment + Vaccine	New mRNA vaccine	Preclinical
 Johnson & Johnson	Vaccine	Covid-19 vaccine	Preclinical
 abbvie	Treatment	lopinavir/ritonavir combination	III
 vaccitech	Vaccine	lopinavir/ritonavir combination	IIb
 REGENERON	Treatment	Monoclonal antibody therapy	Preclinical
 asoletis	Treatment	Combination of two antivirals	I
 Takeda	Treatment	Polyclonal antibody therapy	Preclinical
 HIOHT THERAPEUTICS	Vaccine	Self-assembling vaccine (SAV)	Preclinical
 moderna	Vaccine	mRNA-1273	I
 CanSinoBIO	Vaccine	Covid-19 vaccine	I
 ARCTURUS	Vaccine	Covid-19 vaccine	Preclinical
 AbCellera Lilly	Treatment	Antibody drug	Preclinical
 gsk	Vaccine	Covid-19 vaccine	Preclinical
 inovio	Vaccine	Covid-19 vaccine	Preclinical

Conclusion:

The outbreak of COVID-19 swept across China rapidly and has spread to 85 countries/territories/areas outside of China as of 5 March 2020. Scientists have made progress in the characterization of the novel coronavirus and are working extensively on the therapies and vaccines against the virus. We have summarized the current knowledge of SARS-CoV-2 as follows: Firstly, the emerging pneumonia, COVID-19, caused by SARS-CoV-2, exhibits strong infectivity but less virulence.

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