

# SARS-CoV-2: A brief review

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## Abstract

SARS-CoV-2 also known as COVID-19 is a coronavirus that is genotypically related to SARS-1. It is in the family Coronaviridae, and thus associated with the order Nidovirales. It is spread primarily by the airborne route and is highly contagious but has a low morbidity rate as compared to other airborne organisms. Since the original outbreaks on the Chinese mainland, the virus has spread worldwide. Reports on incidence rates vary. Since like many pandemics the actual morbidity and mortality rates are underreported especially in the initial stages of a pandemic, it may never be known with certainty what the actual numbers are.

## Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2 (COVID-19) has become a worldwide scourge, which has killed in excess of 1 million people to this point. There is little evidence at this time that the pandemic is receding [1]. There are outbreaks in different regions of the world which means that in certain regions, there is the appearance of the disease is disappearing, but in terms of a worldwide health issue, the disease is not yet coming under control. Different countries have taken different routes to deal with the pandemic, from strict quarantines to little control in the hopes of a given population developing “herd immunity”. There is not enough evidence to suggest that either extreme method will contain the virus in the long term. In the near term, quarantine, wearing of PPE in the form of face masks and distancing seem to be effective in preventing the spread of the disease, which is primarily airborne in nature [2].

Human coronavirus was first associated with upper track infections in adults and lower respiratory infections in children [3]. They were first associated with humans in 1960, isolated from a person with a cold [4]. In the past coronavirus infections were limited to small outbreaks that tended to occur in late winter and early spring regardless of geography or population dynamic. Studies in smaller communities showed that the infectious cycle tended to repeat every 2 or 3 years. The SARS agents appear to be an exception. Re-infections are frequent with a given serotype as evidence by the presence of antibody in blood specimens. Coronavirus has over the last 20 years been associated with significant disease outbreaks in Asia and the middle east. Severe Acute Respiratory Syndrome (SARS) and Middle Eastern respiratory syndrome (MERS) became relevant in the 2000's. The SARS-CoV-2 isolate is genetically distinct from other coronaviruses. The available phylogenetic evidence indicates that SARS-CoV-2 is closely related to bat SARS related CoV [5]. This leads to the intriguing possibility that the human form initially was of bat origin, a human was infected, probably by aerosol, and with the rapid mutation that is associated with coronaviruses in general, SARS-CoV-2 developed into the virus sweeping the globe presently. It should be noted that other CoV related forms have also originated with bats [6]. This lends some more credence to the potential hypothesis of origin. Other possibilities include a potential laboratory accident in China, or the potential of a biological weapon, however at this time there is no public information to support these notions. The

current disease has been designated COVID-19 by the WHO, caused by coronavirus SARS-CoV-2.

## Structure

SARS-CoV-2 is a Coronavirus. The *Coronaviridae* are characterized as single stranded positive (+) sense RNA. They are enveloped viruses with a lipid bi-layer surrounding the inner viral core and have surface projections that are 20nm apart. They are spherical and pleomorphic 80-220 nm. The group was first described in 1968 because their morphology and intracellular budding was different than other viruses described at the time. The helical nucleocapsid contains the 30kb, plus sense RNA genome and is coiled in the envelope. The nucleic acid is capped, and polyadenylated [7]. There are 4 proteins associated with this group. The S glycoprotein represents at least a portion of the projections and binds to receptors and induces membrane fusion. It is a class 1 viral transmembrane protein [8]. The size of this protein will vary with various viral types from 1,160 amino acids to about 1,400 amino acids. It exists as a trimer at the surface of the virus. It is primarily responsible for viral entry into a host cell by interaction with host cell surface receptors. This association with host cell receptors gives Coronavirus its host range. The smaller M protein traverses the viral membrane and interacts directly with the nucleocapsid in the virus. It is abundant in the virus and is highly diverse in amino acid content. Viral scaffolding and thus structure are maintained M-M protein interactions. This protein and (pxrimarily) the S protein give the virus it's unusual and distinctive appearance [7]. The N or nucleocapsid protein encompasses the RNA. It is responsible for cell signaling and modulates or regulates the non-specific anti-viral immune response in the form of interferon, which is to say, interferon is down-regulated. The E protein or envelope protein is associated with the viral surface and plays a role in pathogenesis, and assembly and release of the newly formed virus from a host cell. Should a mutation occur where this protein is not present, this leads to altered

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or curtailed virulence of SARS-CoV-2. Coronavirus as a group replicate in a cells cytoplasm and matures at membranes and are ubiquitous in nature. They infect and cause disease in a wide variety of animals, including humans. The diseases they cause are primarily respiratory and intestinal in nature.

The RNA of the Coronavirus group is infectious. The capped RNA is a template for the synthesis of RNA-dependent-RNA polymerase. As with other positive sense ssRNA viruses, the genomic RNA serves as a template for the polymerase to make a minus strand containing 5' poly-U sequence. New plus strands are then produced and a 3' co-terminal strands are created from the minus strand template. As mentioned, assembly occurs in the cytoplasm of infected cells. The N protein assembles with the newly created positive (+) sense strands in the cytoplasm to form helical nucleocapsids. The viral glycoproteins M and S, are translated on the rough endoplasmic reticulum, where the S protein also oligomerizes, and are transported to the Golgi Apparatus where new virus particles form at the plasma membrane and are transported to the cell surface where they are then free to infect other cells (budding). The important E protein is assembled and incorporated at this time also [7,8].

## Pathology and etiology

The human form of SARS-CoV-2 was first isolated from a cluster of infected individuals in Wuhan, China in December 2019. The primary cluster was identified to be from the Huanan South China Seafood Market [9]. It was identified within one month of first reports. SARS-CoV-2 is transmitted from infected individuals through airborne aerosol, and will present in humans with signs including fever, conjunctivitis, sore throat, congestion, cough, nausea, myalgias (sometimes extreme), fatigue (usually extreme) and nausea. Extreme uncontrolled cytokine responses and multiorgan failure characterize more critical cases of acute respiratory distress syndrome.

The virus appears to be most commonly spread by droplet nuclei which require contact points with the nasal track or by an oral route. Evidence also exists for fecal-oral transmission [10]. Although this is a relatively new finding. Regardless of entry portal, it is known that SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE-2) receptor as the principle entry point. Many of the drug treatments are being designed to intercept this part of the infectious pathway. The kidney contains the body's highest concentration of this enzyme however, the second highest are in the lungs. CD-147 (furin) and GRP78 play at least an ancillary role in viral-host cell absorption. Research continues on the exact role these receptors play.

The number of reported cases is in the millions worldwide. Exact numbers of morbidity and mortality are impossible to clearly define and are variable, due to the highly contagious nature of the pathogen and because of imprecise reporting systems in many underdeveloped countries. Fatality rates vary from 1% in South Korea to greater than 7% in Italy. What is also a contributing factor is the change in epicenter location with time. While initially in Wuhan, the virus spread quickly to other regions of the world by air or ship transport. Some anecdotal evidence may indicate that if a population is somewhat isolated from a center containing a major shipping center and international airport, the number of cases tends to be fewer [2].

The virus has a mean incubation period of 5.1 to 6.4 days. The average period prior to symptom onset is 11 days [1]. About 20% of patients who test positive for the virus remain asymptomatic. A clinical study conducted in Iceland where large scale testing was conducted

showed that 50% of infected patients showed no symptoms, but the pre-symptomatic transmission rates may be as high as 60%. Actual viral transmission is between one and three days prior to symptom onset. This provides a clear rationale for distancing as a disease prevention measure. Clearly, there is some conflict in the data, due largely to the relative newness of the disease. As time passes and as more clinical transmission data become available, these questions will be resolved.

The use of masks as a preventive measure has received scrutiny as a result of the Duke University Study, where what became obvious is that use of the N95 mask (or similar) was the only effective medical device for preventing and transmitting disease by the respiratory route [11]. The wearing of masks is effective at reducing the amount of droplet nuclei that an individual may expel. Mask wear and distancing of individuals have to date proved to be the most effective disease interruption mechanisms.

## Treatment

There are no vaccines available for distribution to treat this disease currently. Several companies (Pfizer, AstraZeneca7, BioNTech) have announced plans to expand research and clinical trials on various vaccine candidates which number over 100 currently. The efficacy of the vaccine to induce herd immunity should reach 60% in the general population. One major question concerning vaccines are the types of immune cells produced as a result of either vaccination or infection. There have been any number of incidents of individuals who have re-acquired the disease following initial infection after several months. This is an indication that there is a limited B cell memory of the initial infection. This is similar to other coronaviruses. Research continues in the area [12]. If there is no secondary or anamnestic immune response produced or if it is time limited, vaccination may have limited value. If so, effective protection may require multiple vaccine injections. However, the quality and type of the immune response is speculation at this time. More clinical data need to be established prior to making any long-term determinations. Indeed, only a large, masked Phase 3 clinical trial may yield the answer.

The only approved drug for use in the United States (for emergency use) is Remdesivir, which is designed to block viral replication, which is to say interruption of the viral life cycle early in the infection process [13]. It has been used in Ebola cases as an effective treatment. The drug has been shown to lead to improvement in recovery time as compared to placebo.

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