SARS-CoV-2 and COVID-19

Coronaviruses (CoV), named for the crown-like spikes on their surface (Latin: corona = crown), are RNA viruses that belong to the Coronaviridae family. Coronavirus disease 2019 (COVID-2019) is caused by a novel coronavirus known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and was identified as a pandemic by the World Health Organization (WHO) on March 11, 2020. Until December of 2019, only six different coronaviruses were known to infect humans. Four of these (HCoV-NL63, HCoV-229E, HCoV-OC43 and HKU1) usually caused mild common cold-type symptoms in immunocompetent people. The other two - the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV) - caused severe outbreaks.

In 2002-2003 SARS-CoV epidemic in Guangdon, China, resulted in 10% mortality and in 2012, MERS-CoV cased a devastating pandemic in the Middle East with a 37% mortality rate. In late 2019, the world witnessed another viral outbreak in Wuhan, China, in patients with pneumonia. The virus was discovered to be a novel betacoronavirus and was first called the 2019 novel coronavirus (2019-nCov). When the genomics of the 2019-nCov was sequenced, it shared 79.5% of the genetic sequence of the SARS-CoV that caused the 2002–2003 pandemic and the International Committee on Taxonomy of Viruses renamed the 2019-nCov as SARS-CoV-2.

SARS-CoV2 is an enveloped, non-segmented, positive sense single stranded RNA virus. The diameter of this virus is about 65–125 nm with crown-like spikes on the outer surface as shown in Figure 1. All CoVs that caused epidemics including SARSCoV-2, are believed to originate in bats. However, in most cases, these viruses were transmitted to humans through an intermediate animal host. SARS-CoV started through direct contact with market civet cats and MERS-CoV transmitted directly to humans from dromedary camels. Similarly, SARS-CoV-2 also appears to be transmitted to humans from markets where wild animals are sold and can be transmitted from human to human. The zoonotic source of its transmission is not yet clear. The current hypothesis is that the first transmission occurred between bats and a yet-to-be-determined intermediate host animal (one top candidate is the pangolin anteater).

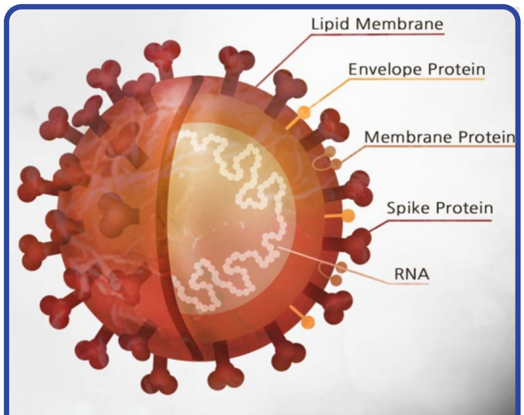

Figure 1. Anatomy of a Virus[1]

Infection: SARS-CoV-2 enters the body of a person through the mouth, nose, and eyes. It attaches to the Angiotensin-converting enzyme 2 (ACE2) receptor embedded in the plasma membrane of cells of the lungs, GI tract, kidneys, and blood vessels. Binding to ACE2 allows the virus to enter the cell via endocytosis or fusion by activation of protease enzymes of the host cell. Once inside the host cell, the RNA genome enters the cytoplasm. The viral positive-sense RNA genome resembles the mRNA of the host cell that is translated directly by the host cell ribosome. The first 20,000 bases of the RNA genome are translated into RNA-dependent RNA polymerase (RdRp) protein. The RdRp then copies the original viral RNA genome to make a negative-sense RNA template. This is used to help make short subgenomic positive-sense RNAs that encode structural and surface proteins by the RdRp again. These subgenomic RNAs are translated by host ribosome into new viral structural and surface proteins that are assembled into new viral particles or virions, which are then released outside of the cell

1 https://bpsbioscience.com/sars-cov-2-coronavirus-covid-19

by exocytosis, taking with them parts of the host membrane that contain spike glycoproteins and other viral membrane proteins. The entire process of entry, replication, and exit of the virus is summarized in Figure 2.

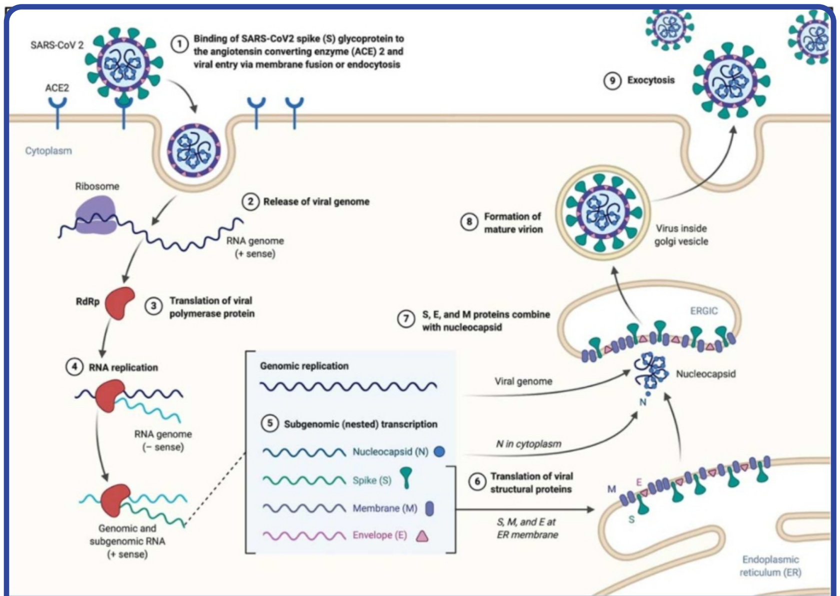

Figure 2. Process of entry, replication, and exit of SARS-CoV-2[2]

Transmission: Respiratory droplets of an infected person (symptomatic, presymptomatic, or asymptomatic) when coughing or sneezing most readily transmits SARS-CoV-2. The spread occurs when droplets are propelled a short distance (generally up to six feet) through the air and deposited on the mucous membranes of the mouth, nose, or eyes of persons nearby. The virus also can spread when a person touches a surface or object contaminated with infectious droplets and then touches his or her mouth, nose, or eye(s). In addition, the virus spreads through aerosols that are airborne, and can travel beyond six feet or by other ways that are still unknown.

Types of Tests: Many nations are employing combinations of containment and mitigation strategies, where early diagnosis of COVID-19 is important to control progression of the illness, limit viral spread within the population, and prevent subsequent infectious waves of viral recurrence in the future.

1) **Diagnostic Testing** plays an important role in the containment of COVID-19, enabling the rapid implementation of control measures that limit the spread through case identification, isolation, and contact tracing. There are two FDA approved diagnostics tests in the US currently in use - *molecular assays* to detect the genetic material using PCR and an *antigen test* to detect proteins that are on the virus surface.

2) **Antibody Testing** looks for antibodies made by the immune system in response to SARS-CoV-2. This test is most useful for determining if someone had COVID-19 in the past. This is not recommended to determine if someone is currently infected, because it takes several weeks for the immune system to produce antibodies.

Treatments and Vaccinations: There are several approaches under investigation to treat COVID-19 as shown in Figure 3. Of these, the investigational antiviral drug remdesivir appears the most promising treatment in development and is the furthest along in testing against COVID-19. Several other existing medications are being tested for their effectiveness such as the HIV medication lopinavir-ritonavir (Kaletra), the antiviral ribavirin, which is used to treat hepatitis C, and Dexamethasone, an anti-inflammatory steriod.

Creating a vaccine requires six stages of development, according to the Centers for Disease Control and Prevention

2 https://doi.org/10.3390/pathogens9050331

(CDC). Those stages include discovering a potential vaccine; testing in cell cultures and in animal models; clinical testing in humans for safety, effectiveness and dosage; applying for approval; manufacturing and quality control. Thus, a safe and effective coronavirus vaccine will likely take at least 12 to 18 months to develop, and possibly longer. There is a large global effort to develop vaccines for protection against COVID-19 and as of early June 2020, at least ten vaccine candidates have entered clinical trials, including phase II trials.

In the meantime, the best option is to reduce disease spread, which requires:

1) Limiting contacts of infected individuals via physical (i.e., social) distancing;

2) contact tracing (i.e., identifying people who may have encountered an infected patient) with appropriate quarantine; and

3) Wearing masks in public. The accumulating evidence indicates that mask wearing reduces the transmissibility per contact by reducing transmission of infected droplets in both laboratory and clinical contexts (Figure 4). Public mask wearing is most effective at stopping spread of the virus when compliance is high. Watch

https://www.nejm.org/doi/full/10.1056/NEJMc2007800.

The decreased transmissibility could substantially reduce the death toll and economic impact while the cost of the intervention is low. Thus, the adoption of public cloth mask wearing is an effective form of source control, in conjunction with existing hygiene, physical distancing, and contact tracing strategies (Figure 5).

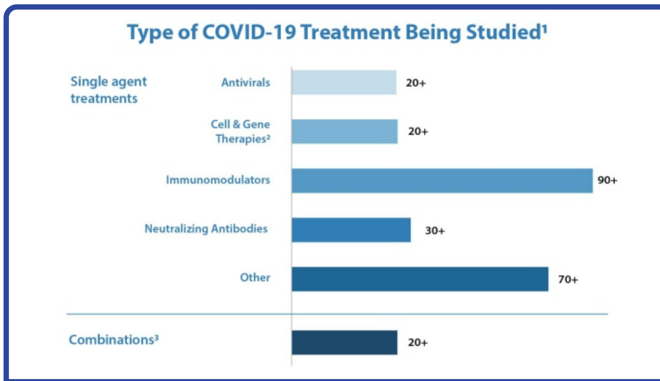

Figure 3. COVID-19 treatments being investigated [3]

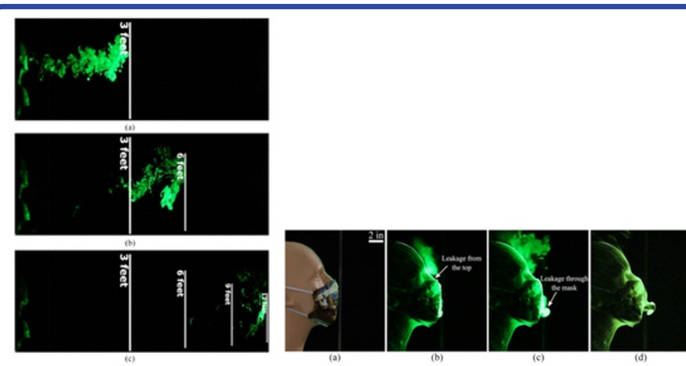

Figure 4. Images published by Verma, Dhanak, and Frankenfield (2020) modeling the spread of droplets with and without masks. The first image shows how far an unimpeded cough can travel at (a) 2.3s, (b) 11s, and (c) 53s. The second images shows how far the same cough travels through a homemade two-layer cotton mask at (b) 0.2s, (c) 0.47s, and (d) 1.68s. [4]

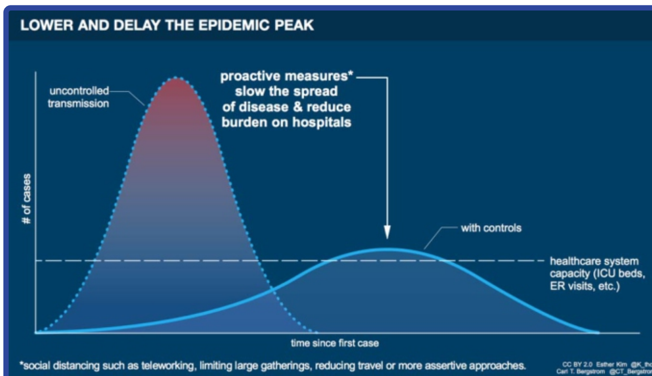

Figure 5. Slowing the spread [5]

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3 https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap
4 Verma S, Dhanak M, Frankenfield J. (2020). Visualizing the effectiveness of face masks in obstructing respiratory jets. Physics of Fluids 32(6):061708. doi:10.1063/5.0016018
5 Kim, Esther, and Bergstrom, Carl T. (2020) https://commons.wikimedia.org/wiki/File:SlowTheSpread.png