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Coronavirus, COVID-19, SARS-CoV-2, droplet, viral transmission, pandemic, outbreak, epidemic

**Abstract**

The world has been in the midst of a swiftly unfolding public health crisis that has turned deadly. The novel coronavirus disease 2019 (COVID-19), has turned out to be a rapidly expanding pandemic affecting the nations of the world. Most governments and their public health authorities worldwide have taken drastic measures to strictly contain the spread of this coronavirus. However, despite the aggressive preventative measures in place, COVID-19 has propagated exponentially across the world. Currently, the accepted mode of disease transmission is by droplets containing the virus. Here we provide epidemiological data in conjunction with biochemical molecular mechanisms of this Severe Acute Respiratory Syndrome- Coronavirus-2 (SARS-CoV-2) and explain the possible alternative modes of disease transmission. Our observed data, biochemical mechanisms, and inferences indicate that COVID-19 has a high probability of transmission through other routes as well, such as indirect routes; viz, fomites and aerosols.

The world is in the middle of a historic public health crisis. As of March 23th, 2020, over a third of the population in the United States were under "stay at home" orders given by state governors to protect the vulnerable and the unexposed. Unprecedented steps have been taken by governments globally to contain the novel coronavirus disease 2019 (COVID-19), a rapidly spreading pandemic. This has resulted in more than 330,000 cases and over 14,500 deaths worldwide (Table 1). The index case of the disease, caused by the Severe Acute Respiratory Syndrome- Coronavirus-2 (SARS-CoV-2) was identified more than three months ago. Since then, public health authorities worldwide have taken aggressive measures to blunt the exponential spread of this coronavirus. Furthermore, several nations including Italy, Spain, and France have imposed nation-wide lockdown measures to enforce social distancing to further prevent the spread of COVID-19 in their respective countries.

While preventative measures have been imposed globally, the observed propagation of COVID-19 has noticeable differences among select nations. Epidemiologic data shows that some nations have exponential increases in disease incidence, while others seem to have "flattened the curve." This raises the questions of whether a full scientific understanding of the modes of transmission of this disease has yet to be attained, and thus whether there are more effective ways to prevent its spread. This brings us to the fundamental question: **Does COVID-19 Spread through Droplets Alone?**

To answer this question we provide epidemiological observational data in conjunction with known molecular characteristics of SARS-CoV-2. We discuss the ability of this novel coronavirus to remain viable on environmental surfaces from hours to days and describe its increased virulence

characteristics compared to the previous SARS-CoV-1. These biochemical and molecular properties likely allow this novel coronavirus to employ indirect methods of transmission including fomites and aerosols in addition to respiratory droplet transmission (Figure 1).

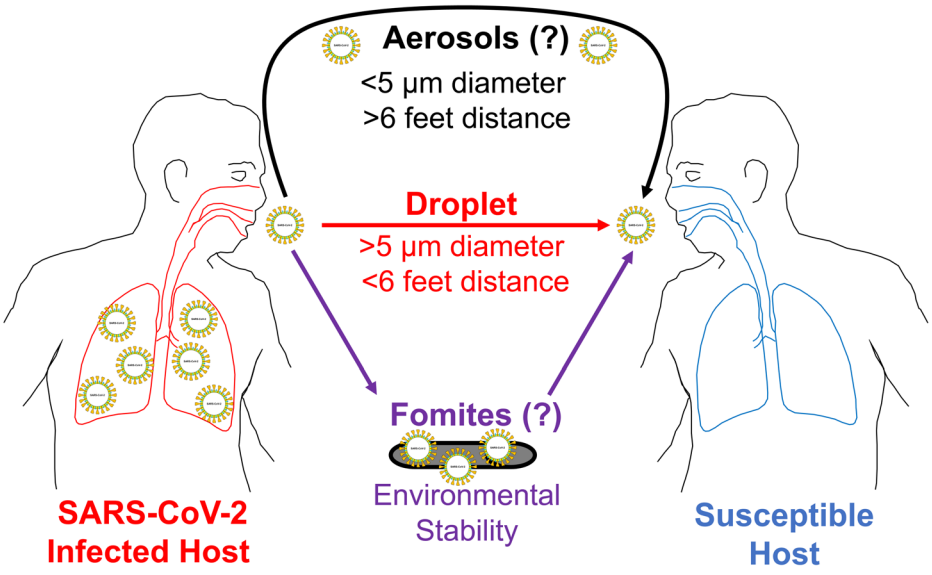


**Figure 1. COVID-19 Potential Modes of Transmission.** This illustration shows three potential ways SARS-CoV-2 can spread from an infected host to a susceptible host. First, it is transmitted person to person (direct contact) through respiratory droplets. These droplets can travel for distances 6 feet or less in air. Second, SARS-CoV-2 is likely transmitted through fomites (indirect contact) for the duration it is viable on environmental surfaces. Third, it is also likely transmitted through aerosols (indirect contact) for distances longer than 6 feet in the air. To establish an infection, SARS-CoV-2 needs to first reach an entry point (eyes, nose or mouth) on a susceptible host.

Public health measures of this aggressive nature have the universal purpose of reducing the exponential rise in incidence rates of disease transmission. Policy regarding these reduction measures has been guided by observations in health outcomes following the 1918 influenza pandemic. Importantly, during this pandemic, some U.S. cities chose more effective measures to address the spread of the disease, resulting in observable differences in mortality rates across the nation [1]. Social distancing is an evidence-based practice to help prevent the transmission of pathogens that are known to spread from person to person within a 3 to 6 feet distance through respiratory droplets [2, 3]. This practice requires individuals in a community to choose behaviors that increase the distance between themselves and others (infected, asymptomatic carriers, or non-infected). This helps reduce the transmission of respiratory droplets containing SARS-CoV-2 and slows the incidence of the disease by reducing the opportunities for potential viral exposures.

Furthermore, this is a great example of how integral the public health system and policies are to the proper function of medical and healthcare systems. Acting swiftly and mobilizing precautionary measures, can substantially aid in flattening the disease incidence curve. Thereby reducing the number of critically ill patients who will need medical treatment -all at the same time. This, in turn, reduces the burden on the healthcare system that takes care of patients presenting with the most feared complication of COVID-19, *i.e.*; severe bilateral pneumonia [4]. This concept now widely referred to as “flattening the curve” gives critically ill patients a fighting chance to survive by obtaining life-saving supportive therapy in hospitals. This, therefore, significantly reduces the mortality rate [1]. If the number of critically ill patients is greater than what can be accommodated in hospitals, many more patients will die due to the lack of life-saving medical attention.

The current consensus regarding the transmission of SARS-CoV-2 is that it spreads person to person through respiratory droplets [5, 6]. Precautions to prevent the spread by droplets as recommended by both the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) are to (1) wash hands with soap, (2) avoid touching viral entry points, such as eyes, nose, and mouth, (3) cover the mouth when coughing or sneezing, (4) wear a facemask if sick and (5) practice social distancing by putting 6 feet of distance between individuals. In addition to these precautions, government-mandated social distancing measures such as (6) state lockdowns and (7) "stay at home" orders are effective ways to minimize the spread of SARS-CoV-2 through droplet transmission. Despite all these aggressive precautionary measures, SARS-CoV-2 has succeeded to establish an exponentially growing pandemic that has spread to almost every nation in the world (Table 1 and Figure 2).

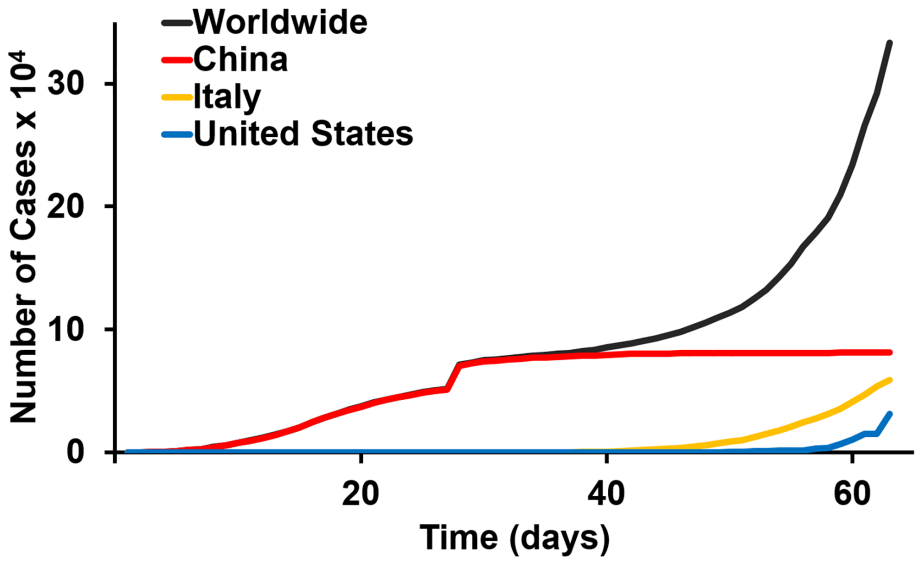


**Figure 2. Number of Cases of COVID-19 Worldwide, China, Italy, and the United States.** The cumulative case total of COVID-19 (SARS-CoV-2) as reported by the World Health Organization daily COVID-19 Situation Reports (1 – 63). This includes cases reported from the 21$^{st}$ of January

to the 23rd of March 2020. As of the 23rd of March, 332,930 cases worldwide, 81,601 cases in China, 59,138 cases in Italy, 31,573 cases in the United States were reported. These three countries reported the highest cumulative cases totals of COVID-19 worldwide and represent the continents of Asia, Europe, and North America.

**Why is SARS-CoV-2 succeeding to spread in this trajectory?**

Certain epidemiological observations may provide evidence to suspect that the spread of SARS-CoV-2 may not be limited to respiratory droplets alone. For example, on the 4th of February 2020, the Diamond Princess Cruise ship carrying 3711 passengers and crew members reported 10 cases testing positive for COVID-19 after their 14-day voyage. As a response to this, the ship was quarantined for 14 days while docked off the coast of Japan. Following this quarantine period, a total of 634 cases reportedly tested positive for COVID-19, despite droplet precautions and social distancing principles practiced on board [7]. In retrospect, public health officials acknowledge this was not the best practice implemented to contain COVID-19. Additionally, public health officials responded differently to the Grand Princess Cruise ship off the coast of Oakland California, based on suspicions that the dramatically widespread transmission of fomites or COVID-19 aerosols may have been exacerbated by interconnected central ventilation between ship cabins [8]. Public health officials removed all susceptible and unexposed passengers from this cruise ship, which resulted in a significantly lower number of COVID-19 cases [8].

Tragically, another story that is unfolding in the COVID-19 pandemic is occurring within the country of Italy, which currently maintains a mortality rate of 9.3% (Table 1). Once the number of COVID-19 positive cases surpassed 5000, the government of Italy imposed a nationwide

lockdown measure on the 9th of March (Figure 3, black arrow). However, even after these measures were in place for over two weeks, the number of cases of COVID-19 continued to rise exponentially, surpassing 50,000 cases by the 22nd of March (Table 1 and Figure 3). This may suggest that Italy responded far too late to implement preventative measures that could have flattened the curve. Or, this example may suggest that even amidst the aggressive precautionary measures taken to reduce droplet transmission, that aerosol transmission may have also occurred, which may more effectively explain this outcome. These observations are not limited to just Italy. Most of the European nations are currently experiencing an exponential increase in the incidence rate of COVID-19 despite many stringent precautionary measures employed over the past several weeks (Figure 3). These epidemiological observations in the rapid spread of the disease across nations practicing droplet precautions strongly suggest there may be other alternative modes of disease transmission (Figure 1).

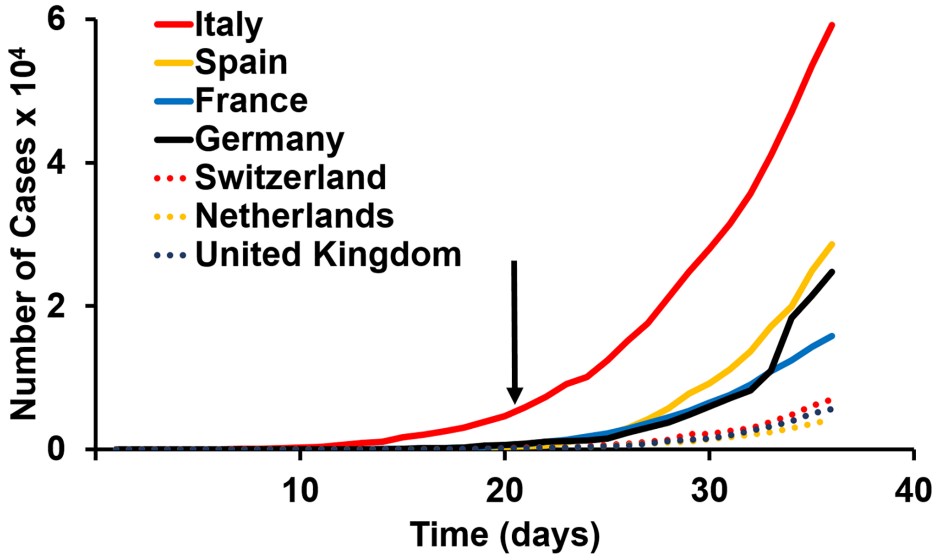


**Figure 3. Number of Cases of COVID-19 in Select Countries in the European Region.** The cumulative case total of COVID-19 (SARS-CoV-2) as reported by the World Health Organization

daily COVID-19 Situation Reports (28 – 63). This includes cases reported from the 17th of February to the 23rd of March 2020. As of the 23rd of March, 59,138 cases in Italy, 28,571cases in Spain, 15,821 cases in France, 24,772 cases in Germany, 6,971 cases in Switzerland, 4,204 cases in Netherlands and 5,687 cases in the United Kingdom were reported. The black arrow indicates the 9th of March, 2020, the date Italy was placed under mandatory lockdown by their government.

**What are other alternative modes of disease transmission contributing to the spread of COVID-19?**

I. Recent studies have indicated that SARS-CoV-2 demonstrated 10-20 times greater affinity to angiotensin-converting enzyme 2 (ACE2) receptors compared to SARS-CoV-1, making it a much more virulent virus [9, 10]. This means ***fewer SARS-CoV-2 virions are necessary*** to establish an infection in humans. This in part, could explain the rapid spread of the disease worldwide compared to the 2002-2003 SARS outbreak that infected approximately 8,100 individuals.

II. The primary mode of transmission of SARS-CoV-1 in the 2002-2003 outbreak was by respiratory droplets up to a distance of about 6 feet [3, 11]. However, SARS-CoV-1 has also shown to be viable on a variety of common surfaces under environmental conditions up to 96 h post-exposure [12, 13]. SARS-CoV-2 was recently shown to remain viable on average for about 6.8 h on plastic surfaces and about 5.6 h on stainless steel surfaces, and viable virions were detected up to 72 h post-exposure [14]. These studies have demonstrated that SARS-CoV-2 can ***remain viable in the environment much longer*** than most other viruses transmitted through respiratory droplets.

The ability of SARS-CoV-2 to remain viable longer on surfaces taken together with its higher virulence in establishing an infection makes it very likely that this coronavirus uses other modes of transmission in addition to respiratory droplets (Figure 1). Remaining longer in the environment may mean this coronavirus can easily transmit through ***indirect contact transmission***. This is can be either a certain level of airborne spread or vehicleborne (fomites) transmission. Pathogens like influenza virus and rhinovirus that are usually spread through respiratory droplets have some airborne transmission properties making it plausible that SARS-CoV-2 may have such characteristics as well [2, 15, 16]. Such additional modes of transmission can help further explain the observations made on the Diamond Princess Cruise ship, in Italy and other European nations. On the cruise ship, contaminated surfaces and utensils (fomites), and aerosolized viral particles traveling beyond 6 feet could have exacerbated the volatile spread of COVID-19. In Italy having houses or other domiciles in close proximity to one another may have transmitted the disease even with a limited level of aerosolization. This example may also greater explain the current exponential spread of SARS-CoV-2 in many European nations and in the United States that are aggressively practicing social distancing.

**How can the spread of the Coronavirus be better prevented?**

Today, the world is facing a certain deadly disease to which there is no cure currently nor a vaccine. Based on the aforementioned findings, if SARS-CoV-2 is also transmitted through indirect contact, greater and additional, yet practical methods of precaution must be taken. There are ways to help prevent such spread. (1) First, it is important to follow all droplet precautions including washing hands with soap or using an alcohol-based hand sanitizer for 20 to 40 seconds, (2) protecting viral entry points, (3) covering one’s mouth when coughing or sneezing, and (4)

appropriate social/physical distancing. In addition, (5) constantly disinfecting contact surfaces can eliminate the risk of fomite-based transmission. (6) Furthermore, to prevent the possible spread of aerosolized SARS-CoV-2 infections, we will need to reevaluate the current recommendations of 6 feet of physical separation between individuals but possibly increase it further. Finally in areas of increased risk of COVID-19 transmission such as hospitals and patient care facilities, (7) an appropriately fitted N95 respiratory (facemask), with other personal protective equipment (PPE) and (8) expanded use of special air handling and ventilation systems (e.g. AIIRs). This can help contain and safely remove SARS-CoV-2 likely transmitted through aerosolization [17, 18].

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**Table Legend**

**Table 1.** Mortality Rates of COVID-19 as of March 23rd, 2020 in Select Regions and Countries.

| Country | Number of Cases[1] | Mortality Rate (%)[2] |
|---|---|---|
| ***Western Pacific Region*** | | |
| China | 81601 | 4.0 |
| South Korea | 8961 | 1.2 |
| Japan | 1089 | 3.8 |
| Malaysia | 1306 | 0.8 |
| Singapore | 445 | 0.4 |
| Philippines | 380 | 6.6 |
| Australia | 1396 | 0.5 |
| ***European Region*** | | |
| Italy | 59138 | 9.3 |
| Spain | 28571 | 6.0 |
| France | 15821 | 4.3 |
| Germany | 24772 | 0.4 |
| Switzerland | 6971 | 0.9 |
| Netherlands | 4204 | 4.3 |
| United Kingdom | 5687 | 4.9 |
| ***South-East Asia Region*** | | |
| Thailand | 721 | 0.2 |
| India | 415 | 1.7 |
| Sri Lanka | 82 | 0 |
| ***Eastern Mediterranean Region*** | | |
| Iran | 21638 | 7.8 |
| United Arab Emirates | 153 | 1.3 |
| ***North American Region*** | | |
| United States of America | 31573 | 1.3 |
| Canada | 1384 | 1.4 |
| **Worldwide (All Cases Globally)** | **332930** | **4.4** |

[1] Number of cases of COVID-19 as reported by the World Health Organization (WHO) in their Coronavirus disease 2019 (COVID-19) Situation Report – 63, published on March 23rd, 2020.

[2] Mortality rate (%) calculated by taking the ratio of the total number of deaths and the total number of cases reported by the WHO for each country in their Coronavirus disease 2019 (COVID-19) Situation Report - 63 published on March 23rd, 2020.

**Figure Legend**

**Figure 1. COVID-19 Potential Modes of Transmission.** This illustration shows three potential ways SARS-CoV-2 can spread from an infected host to a susceptible host. First, it is transmitted person to person (direct contact) through respiratory droplets. These droplets can travel for distances 6 feet or less in air. Second, SARS-CoV-2 is likely transmitted through fomites (indirect contact) for the duration it is viable on environmental surfaces. Third, it is also likely transmitted through aerosols (indirect contact) for distances longer than 6 feet in the air. To establish an infection, SARS-CoV-2 needs to first reach an entry point (eyes, nose or mouth) on a susceptible host.

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