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Shifting Approach to Environmentally Mediated Pathways for Mitigating COVID-19: *A Review of Literature on Airborne Transmission of SARS-CoV-2*

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ABSTRACT

Coronavirus disease 2019 (COVID-19), caused by the novel coronavirus SARS-CoV-2, has been confirmed in over 10,000,000 individuals worldwide and has resulted in more than 500,000 deaths in a few months since it first surfaced. With such a rapid spread it is no surprise that there has been a massive effort around the world to collectively elucidate the mechanism by which the virus is transmitted. Despite this, there is still no definitive consensus regarding droplet versus airborne transmission of SARS-CoV-2. Public health officials around the world have introduced guidelines within the scope of droplet transmission. However, increasing evidence and comparative analysis with similar coronaviruses, such as severe acute respiratory syndrome (SARS-CoV-1) and middle eastern respiratory syndrome (MERS), suggest that airborne transmission of SARS-CoV-2 cannot be effectively ruled out. As the data supporting COVID-19 airborne transmission grows, there needs to be an increased effort in terms of technical and policy measures to mitigate the spread of viral aerosols. These measures can be in the form of broader social distancing and facial covering guidelines, exploration of thermal inactivation in clinical settings, low-dose UV-C light implementation, and greater attention to ventilation and airflow control systems. This review summarizes the current evidence available about airborne transmission of SARS-CoV-2, available literature about airborne transmission of similar viruses, and finally the methods that are already available or can be easily adapted to deal with a virus capable of airborne transmission.

Keywords: COVID19, Airborne transmission, Droplet transmission, Aerosol transmission, SARS-CoV-2, Heat Inactivation, Infection Prevention, Ventilation system

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INTRODUCTION

On March 11th, 2020, coronavirus disease 2019 (COVID-19) was designated by the World Health Organization (WHO) as a pandemic. It has since been confirmed in over 10 million cases worldwide and has resulted in more than 500,000 deaths.[1] Despite the widespread investigation of COVID-19, many aspects of the disease such as the severity, demographic preference, and transmission of the disease, are still under contention. The Centers for Disease Control and Prevention (CDC) characterizes the transmission of infectious agents via three mechanisms: direct or indirect contact, droplet, or airborne route.[2] While efficient human to human transmission of COVID-19 is undisputed,[3] the extent of this mode of transmission has yet to be fully confirmed. Current guidelines from the WHO and CDC have resigned to treat COVID-19 as a droplet transmitted disease, thereby recommending facial coverings and a distance of 2 meters between individuals.[4,5] However, analysis of previous coronaviruses, increasing evidence by way of case study, and incoming, but limited, empirical data shows that not only are droplet precautions inadequate, but airborne precautions merit aggressive implementation.[6,7,8]

There is commonly known evidence related to the aerosol transmission of various viral pathogens, such as Influenza virus, Rhinovirus, Adenovirus, Measles virus, Respiratory Syncytial virus, and Ebola virus. Of more importance, is the wealth of evidence concerning coronaviruses such as SARS-CoV and MERS. Given the high level of genetic conservation between the novel SARS-CoV-2 and previously studied coronaviruses,[9] there is mounting reason to infer that SARS-CoV-2 may also be distributed via aerosol transmission. Transmission via airborne particles 5 micrometer (μm) or less in size from asymptomatic carriers can help understand the unprecedented spread of this novel disease.[10]

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Although the current evidence regarding airborne transmission needs to be interpreted with caution, it should at least encourage the adoption of simple measures that can mitigate aerosol dispersion. At a general population level, the use of face masks should be universal, as it has been associated with a decline in new cases where implemented.[11] Resourceful attempts have been made to repurpose surgical personal protective equipment (PPE), but to our knowledge, none have been successful in preventing the inhalation of potentially virulent aerosols.[12] Because of the documented susceptibility to heat of coronaviruses,[13] promising strides have been made in deactivating COVID-19 by applying high, yet tolerable, temperatures to the upper respiratory tract.[14] Because of the potential of ultraviolet light, particularly type C (UVC), in deactivating pathogenic microbes [15-17], low dose UVC is a candidate for widespread implementation in hospitals, doctors' offices, and other high-risk areas [18]. Lastly, properly designed ventilation systems inside buildings can be an effective tool to curtail airborne infection. Inventive approaches to developing portable, low cost, negative pressure systems are beginning to appear regularly.[19,20] Critical elements of ventilation that influence airborne transmission include ventilation rate, flow direction, and airflow pattern.[21]

The objective of this review has been to explore and summarize the rapidly emerging literature regarding airborne transmission of SARS-CoV-2, the available literature regarding airborne transmission of related viruses that have been involved in previous outbreaks, and finally the methods and technologies that are already available or can be easily adapted to deal with a virus capable of airborne transmission.

Transmission of Viral Pathogens

The CDC characterizes the transmission of infectious agents via three mechanisms: direct or indirect contact, droplet, or airborne route.[2] Direct or indirect contact involves transmitting the pathogen from one person to another with or without a contaminated intermediate, respectively.[22] Droplet transmission involves the expulsion of droplet particles, 5 µm or greater in diameter, from the respiratory tract. These projected droplets can directly settle on the mucosae of an exposed individual or they can reside on surfaces, such as door knobs, to be picked up later by hand.[23] In contrast, airborne transmission results from the inhalation of droplet nuclei. These small particles are distinguished by having a diameter of 5 µm or less. Notable infectious agents that spread via the airborne route include Influenza, Measles, and Tuberculosis, among others.[23] The formation of infectious bioaerosols, in the general public, are linked to multiple processes such as expiratory activities of humans, showering or use of tap water, sewage aerosolization from toilets, and sewage transport through pipe systems, wet-cleaning of indoor surfaces, and agricultural spraying of 'gray' water.[24] Aerosol formation in healthcare settings, as listed by the CDC, is possible via specific procedures such as open suctioning of airways, sputum induction, cardiopulmonary resuscitation, endotracheal intubation and extubation, non-invasive ventilation (e.g., BiPAP, CPAP), bronchoscopy, and manual ventilation.[5] Currently, the WHO applies the greater or less than 5 µm size of droplet nuclei to differentiate between droplet transmission and airborne transmission.[25] However, this dichotomy comes with limitations. Particles capable of projecting from the respiratory tract and being inhaled by a susceptible individual can be both greater and lesser than 5 µm in size. Aerosol plumes generated from coughing, sneezing, or speaking, can range from less than 0.1 µm to greater than 100 µm and lodge directly into airway, tracheobronchial, or alveolar locations.[26] These aerosols are capable of remaining suspended in gas or air for extended periods. Furthermore, a recent review by Bahl et al. addresses various studies exploring horizontal droplet distance by presenting evidence that infectious particles may travel distances up to 26 feet.[4] While large droplets may typically settle within 3 to 6 feet of an individual, other smaller droplets are capable of remaining suspended, traveling through a room or to other rooms, and landing 20 to 26 feet away.[27]

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There is already ample evidence related to the aerosol transmission of common viruses, such as Rhinovirus, Adenovirus, Measles virus, Respiratory Syncytial Virus, and Ebola Virus.[28-32] Indeed, literature regarding the aerosol transmission of Influenza virus and Coronavirus has become extensively available following the 2003 outbreak of SARS-CoV-1.[33] In the case of Influenza virus, a study by Francoise et al. confirmed the presence of airborne transmission by collecting aerosol samples in different areas of an emergency department. Their study found that, throughout the healthcare environment, airborne virus particles were present, and approximately 53% of these particles were 4 μm in size or below.[34] In the case of MERS, a viral presence was found in 4 of 7 air samples from 2 patient rooms, a patient restroom, and a common corridor.[35] Finally, in the case of SARS-CoV, a robust analysis of the first 187 cases in the Amoy Gardens housing complex found that aerosol transmission of viral particles accounted for a significant amount of the community outbreak.[36] Additional retrospective studies show the prevalence of SARS-CoV aerosol transmission within healthcare settings, housing complexes, and aircraft.[37-40]

Given the high level of genetic conservation between the novel SARS-CoV-2 and the viruses mentioned above—particularly MERS and SARS-CoV—there is mounting reason to infer that SARS-CoV-2 may also be distributed via aerosol transmission.[9]

Evidence/Characteristics of SARS-CoV-2 Airborne Transmission

Recent literature has suggested that an increasing number of SARS-CoV-2 cases occur via inhalation of aerosols produced by asymptomatic carriers.[10] These aerosols, produced by way of coughing, sneezing, and even speaking, can linger in indoor air for some time and be inhaled later by other individuals.[41] This stability of the virus poses a challenge to healthcare workers and the general population to limit the proliferation of the disease.

SARS-CoV-2 has an initial tropism for the upper respiratory tract, where it exhibits a large amount of active viral pharyngeal shedding in contrast to SARS-CoV.[42] This affinity for the upper respiratory tract presents with mild-to-asymptomatic symptomology and increases the potential dispersion of fine aerosolized infectious particles. To further explicate the similarities between SARS-CoV-2 and SARS-CoV, van Doremalen et al. investigated the aerosol and surface stability of each virus. Their results not only indicated that aerosol transmission of SARS-CoV-2 was plausible, but that the virus could remain suspended in the air for over 3 hours, similar to SARS-CoV.[41] Together these findings suggest that populations may be susceptible to SARS-CoV-2 superspreading events via aerosol, similar to the SARS-CoV Amoy Gardens housing complex incident.

Indeed a small but growing number of case reports are beginning to appear in support of airborne transmission.[8] Many of these reports originate in China, which experienced a high caseload early in the pandemic, while a few high profile "superspreading" events appear in the United States.[43-46] Of note, was a choir practice event that resulted in 45 of 60 choir members being infected.[45] Interestingly, choirs have been linked to multiple outbreak events in the United States, possibly due to both an increase in droplet projection and an increase in droplet nuclei dissemination through aerosolization.[47] These "superspreading" events are likely the result of a few asymptomatic individuals, presumably in the early pharyngeal shedding stage, expelling aerosolized droplet nuclei while simply speaking or breathing. As asymptomatic individuals, it is less likely that these "silent shedders" are coughing or sneezing at a rate to justify only droplet transmission.[10] A plausible explanation for their high infectivity lies in the ability of SARS-CoV-2 to aerosolize in droplets smaller than 5 μm. Indeed, a study by Leung et al. showed that seasonal coronaviruses were more commonly emitted as aerosols, even in ordinary tidal breathing.[48] Furthermore, it is estimated that merely 1 minute's worth of loud speaking, let alone singing, could create over 1000 virion-containing aerosol particles.[49] A report published by Li et al., found that 79% of SARS-CoV-2 cases in China were via an asymptomatic carrier, which makes it unlikely that they were producing large infectious droplets and further support aerosolization as a mechanism for the transmission of SARS-CoV-2. [50]

As stated in a commentary of aerosolized transmission by Anderson et al., little empirical data exists, and a broader initiative is needed regarding the exact aerodynamics of SARS-CoV-2 airborne transmission.[8] This is bolstered by a statement made by the National Academy of Science that while little SARS-CoV-2 specific research is available for airborne transmission, the current studies comply with the idea that the virus is aerosolized via normal tidal breathing.[51]

Mitigation of Airborne Transmission

Methods to mitigate the spread of infectious SARS-CoV-2 aerosols are wide-ranging in ease, time, cost, and universality of implementation. Currently, the CDC, WHO, and European Centre for Disease Prevention and Control have issued guidelines primarily intended to limit the spread of SARS-CoV-2 droplets.[4] While the CDC has recommended precautions for airborne transmission, it only advocates for them in healthcare settings during aerosol-generating procedures.[5] For the general public, a 2-meter spatial separation is recommended to limit the possibility of droplet transmission. Unfortunately, even droplets (> 5 μm) have been shown to spread up to 8 meters,[4,52] suggesting that the current recommendation of 2-meter distance may have limited effectiveness even for droplet transmission.

The use of face masks by the general population has been associated with mitigation in the spread of SARS-CoV-2. A recent retrospective analysis by Lyu & Wehby of 15 states and Washington D.C. showed that after mandating public use of face coverings, the SARS-CoV-2 growth rate decreased by 0.9, 1.1, 1.4, 1.7, and 2.0 percentage points in 1-5, 6-10, 11-15, 16-20, and 21+ days respectively.[11] Although this may have averted an estimated 230,000-450,000 cases in the general population, simple face coverings are not enough to adequately protect high-risk individuals such as health care workers from aerosol exposure. Because of reported aerosol spread in previous coronavirus outbreaks, SARS-CoV, and MERS, the WHO at the time recommended masks in low-risk situations and respirators in high-risk situations while the CDC recommended respirators in both situations.[53-56] Nevertheless, this time round, in spite of the evidence supporting aerosol transmission of SARS-CoV-2, the CDC recommends only masks for low-risk situations and reserves respirators for high-risk, aerosol-generating procedures. These procedures are listed as open suctioning of airways, sputum induction, cardiopulmonary resuscitation, endotracheal intubation and extubation, non-invasive ventilation (e.g., BiPAP, CPAP), bronchoscopy, and manual ventilation.[5] Much of the hesitancy to universally mandate respirator devices in healthcare settings comes from the worry of supply shortages.[24]

Methods of Viral Inactivation

One pathway to eliminate aerosol transmission of SARS-CoV-2 is available via heat inactivation. Rabenau et al. investigated the stability and inactivation of SARS-CoV in 2004 and found that a temperature of 60°C was highly effective in reducing virus titers to below detectability.[13] Using this information, Knio et al. developed a thermal treatment for inactivating SARS-CoV-2 that resides in droplet nuclei.[14] They showed that air heated to 80-90 degrees Celsius is tolerable to the respiratory tract and successfully demonstrated a proof of concept worthy of further exploration in the battle against SARS-CoV-2 and potential future viral pandemics – although the widespread acceptance and implementation of their proposed method is likely to be challenging.

Another approach to virus inactivation is ultraviolet light (UV). Of the many types of UV light, UVC, at the range of 315-380 nm, has the most potent antimicrobial and antiviral properties.[15,16] A recent review by Heßling et al analysing data from 30 publications concluded that UVC radiation has been effective against all previous coronavirus strains. Although none of the publications deal with the novel SARS-CoV-2 strain, the structural similarities of the coronavirus family are strong enough to believe that UVC will be an effective weapon against SARS-CoV-2 and any subsequent mutations.[17] Indeed, previous technological innovations in the delivery of bactericidal and virus inactivating UVC to an infected area without damage to mammalian skin are worth revisiting. For example, in 2017, Welch et al. developed the use of far-UVC light (207-222 nm) to inactivate over 95% of the aerosolized H1N1 influenza virus.[18] Using a continuous low dose, they were able to avoid the carcinogenic and cataractogenic effects of UV radiation and sufficiently reduce the spread of airborne-mediated microbial disease. Developments such as this hold value in public settings such as hospitals and doctors' offices, schools, airports, and beyond. However, if direct exposure to the human can be avoided, by engineering devices that contain UVC inside the device when treating air with it, a higher 254 nm UVC can be used as they have minimal ozone production, if any. Continuous progress in developing UV mediated solutions should garner much attention in future attempts toward pandemic mitigation.

Improving ventilation and air disinfectant techniques are also viable ways to explore SARS-CoV-2 aerosol mitigation.[57] Observational evidence of a case in Guangzhou, China has shown that air conditioning played a role in the transmission of SARS-CoV-2 between an infected carrier and three family clusters while eating in a restaurant. Investigators concluded that transmission of the virus was facilitated by the ventilation system.[58] The role of ventilation systems has immense implications in viral spread, given the growing evidence supporting airborne transmission of SARS-CoV-2 . Therefore, interior ventilation rate and air purification in an enclosed space are of crucial importance in restricting the spread of aerosolized viruses.[59] Following the appearance of an infection cluster in a call center in Seoul, South Korea, the Korean Ministry of Employment and Labor proposed the installation of air purifiers at the floor of the call center area with exhausts at face level.[60]

In recognition of the importance, and scarcity, of adequately ventilated patient areas, Lynch & Goring published a five-step guide to transforming standard patient rooms to negative pressure spaces. These five steps involve estimating total room volume, ventilation and differential pressure, installing supplemental exhaust ventilation through dedicated exhaust portals, increasing efficiency of filtration, keeping doors closed, and following the Infectious Disease Prevention Guidelines for health care workers.[61] Additionally, many ingenious portable isolation chambers have begun to appear to prevent airflow amongst individual patients. For example, Cubillos et al. created a cubic chamber made of widely accessible materials that produce an enclosed continuous negative airflow environment through vacuum mechanisms around the patient.[19] Adir et al. have created a similar negative pressure canopy with multiple filtering units. This contraption allows the administration of noninvasive ventilation, continuous positive airway pressure, and high-flow nasal cannula, to SARS-CoV-2 patients with minimal risk to healthcare workers.[20] Innovative filtering materials involving electrostatically charged nanofibers are also being developed that have potential applications to reduce aerosol spread via building ventilation.[62] Higher ventilation rates are believed to reduce the transmission of disease by diluting contaminated air inside a space.[63] The current recommended minimum ventilation rate for airborne infection isolation rooms by the CDC is 12 air changes per hour.[64] Properly directing airflow from clean zones to dirty zones is vital to prevent virulent aerosols from traversing between rooms.[61] Airflow patterns can be further subdivided into downward ventilation, displacement ventilation, and mixing ventilation, with an improved downward ventilation system having the greatest performance in eliminating droplet nuclei that could cause infection.[65] Conceptual framework for this has been laid down by Luo *et al* who have elicited the absolute reduction of actual SARS-CoV-2 by treating the air with a specialized biodefense indoor air protection system.[66]

CONCLUSION

There is sufficient evidence that confirms airborne transmission of SARS-CoV-2. Quantitative studies to directly measure concentrations of aerosolized SARS-CoV-2 face numerous limitations. It is incredibly challenging to address the multiple variables that affect the production and airborne transmission of respiratory viruses. These include airflow, humidity, temperature, spatial patterns, and minimum virus titers, and length of exposure needed to cause infection among susceptible individuals. While further research is necessary in all these areas, the aforementioned studies, comparisons with other viruses, and growing cases warrant a more urgent action beyond simply relegating transmission to being purely droplet spread. Therefore, guidelines accounting for airborne transmission of SARS-CoV-2 should be established and technology deployed immediately. Leveraging research advancements in UV, heat inactivation, and improved ventilation technologies are vital to creating sustainable methods in virus spread mitigation indoors. Search for cutting-edge applied physics based inventions with biodefense characteristics will find a place in future pandemics.

Data Availability

No data are associated with this article

Competing Interests

No competing interests were disclosed.

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