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EDITORIAL

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COVID-19 and the workplace: Research questions for the aerosol science community

The global Coronavirus Disease (COVID-19) pandemic caused by the SARS-CoV-2 virus has raised many urgent questions about the transmission of this disease, including the possible roles of aerosols containing SARS-CoV-2. This is particularly true in workplace settings where workers may encounter customers and coworkers who are infected with COVID-19 and where aerosols can be produced in a variety of ways. Research by the aerosol science community is needed to learn more about whether SARS-CoV-2 can spread by infectious aerosols and about the effectiveness of different protective measures. The purpose of this commentary is to present some of the questions surrounding aerosols containing SARS-CoV-2 and to provide suggestions for future research topics.

How much SARS-CoV-2 aerosol is generated by coughing, sneezing, talking, singing, and breathing, and what are the implications for transmission?

Transmission of SARS-CoV-2 can occur via respiratory droplets produced by infected individuals when talking, singing, coughing, breathing, or sneezing (CDC 2020a; Hamner et al. 2020; WHO 2020). Thus, public health guidance has focused on the use of face masks or cloth face coverings, physical distancing, frequent surface disinfection, and hand hygiene, especially in areas with significant community-based transmission (CDC 2020a). Respiratory protection with an N95 respirator or an equivalent or higher-level respirator is recommended for healthcare providers performing aerosol-generating procedures such as intubation of patients who may be infected (CDC 2020b). However, small aerosol particles also are emitted by people during normal breathing and talking, even in the absence of a cough, with the amount and size distribution of aerosol particles varying greatly from person to person (Asadi et al. 2019; Gralton et al. 2011). Aerosols containing other viruses have been found in a variety of settings and detected in the coughs and exhaled breath of infected patients (Judson and Munster 2019; Shiu, Leung, and Cowling 2019; Tellier et al. 2019). Some authors have suggested that short-range airborne transmission of SARS-CoV-2 may be possible under some circumstances (Anderson et al. 2020; Morawska and Milton 2020).

A few studies have examined aerosols containing SARS-CoV-2. Ma et al. (2020) detected SARS-CoV-2 in the exhaled breath of COVID-19 patients. van Doremalen et al. (2020) found that SARS-CoV-2 in experimentally generated aerosols ($<5\,\mu$m) remained viable for at least 3 h. Santarpia et al. (2020) collected high volume air samples in biocontainment and quarantine units housing SARS-CoV-2 infected persons at the University of Nebraska Medical Center and found aerosols containing SARS-CoV-2 genetic material in 63% of samples from isolation rooms of patients, including from samplers placed >6 feet from the patient. In another study, Liu et al. (2020) sampled aerosols at multiple locations throughout two hospitals in Wuhan during a COVID-19 outbreak. The authors reported that the sizes of aerosol particles containing SARS-CoV-2 RNA ranged from below $0.5\,\mu$m to larger than $2.5\,\mu$m, with most being in two size ranges (aerodynamic diameter between 0.25 and $1.0\,\mu$m and $>2.5\,\mu$m). They also calculated a normalized particle deposition rate of between 31 and 113 copies $m^{-2}h^{-1}$ inside an intensive care unit room. However, the concentrations of SARS-CoV-2 in most of the environmental aerosol samples were very low or undetectable and the ability of the airborne virus to cause infection was not assessed. The particle size is the most important factor determining the behavior of airborne particles, and more information about the amount of potentially infectious SARS-CoV-2 contained in large ballistic droplets that settle quickly and in smaller droplets that can remain airborne is urgently needed.

Many questions remain about the possible transmission of SARS-CoV-2 by aerosol particles. How much airborne virus is expelled by people? What is the particle size distribution? How do speaking, coughing, and breathing affect the emission rate? Is the airborne virus infectious? Answers to these questions will help to better understand the roles of droplet and aerosol transmission of SARS-CoV-2 and inform public health recommendations.

Are potentially infectious aerosols produced by toilets containing human waste with SARS-CoV-2?

Numerous research studies have shown that the flushing of toilets can generate aerosols that could lead to the transmission of pathogens (Aithinne et al. 2019; Johnson et al.

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2013). However, in the case of SARS-CoV-2, the potential contribution of this route of transmission is unclear. SARS-CoV-2 RNA has been found in the feces of diagnosed patients (Chen et al. 2020; Lo et al. 2020), and viable SARS-CoV-2 virus has been detected in feces from patients using culture and electron microscopy techniques (Wang et al. 2020; Xiao et al. 2020). SARS-CoV-2 viral RNA was found in feces of children during their recovery period (Xu et al. 2020; Zhang et al. 2020). SARS-CoV-2 genomic RNA also has been detected in water treatment plants in the Netherlands (Lodder and de Roda Husman 2020).

Airborne SARS-CoV-2 RNA has been detected in higher concentrations in patient bathrooms compared to other locations (Ding et al. 2020; Liu et al. 2020). Furthermore, other viruses from the *Coronaviridae* family have been found to remain infectious while in feces for up to 24 h at room temperature (Thomas et al. 2015). More work is needed to better understand the possible production of SARS-CoV-2 aerosols by toilet flushing, the size distribution of the aerosol, the infectivity of the virus in the aerosol, and the risk that exposure to these aerosols may pose to healthcare workers and others.

How much risk do aerosol-generating medical procedures on patients with SARS-CoV-2 present to healthcare workers?

Certain medical procedures such as endotracheal intubation, airway suctioning and noninvasive ventilation, and dental procedures such as cleaning and tooth preparation, produce infectious aerosols when performed on patients with respiratory infections such as COVID-19 and thus present a danger of airborne disease transmission to healthcare workers (Harrel and Molinari 2004; Judson and Munster 2019; Wilson et al. 2020). However, for many procedures little is known about the quantity or size distribution of infectious aerosols or the risks to workers. For example, a few studies suggest that cardiopulmonary resuscitation (CPR) on patients with SARS-CoV-1 may have led to airborne disease transmission to workers, but none have directly shown that CPR produces infectious aerosols (Couper et al. 2020). Pregnant patients with respiratory infections breathe deeply, cough and shout while in labor, which suggests that people nearby may be exposed to infectious aerosols, but this has not been studied and labor and delivery are not currently listed as aerosol-generating procedures by the World Health Organization or CDC (Palatnik and McIntosh 2020). For procedures known or thought to produce infectious aerosols, techniques are needed to reduce exposure. For example, noninvasive ventilation may be an alternative for intubation for some patients needing respiratory support, but it may have placed workers at greater risk of airborne transmission when used with SARS-CoV-1 patients (Tran et al. 2012). More information is needed about the amount and size distribution of infectious aerosols produced by different aerosol generating procedures, the risks that these aerosols pose to healthcare workers, and the best methods for protecting these workers.

Which engineering control methods are most effective to prevent exposures to SARS-CoV-2 through droplet, fomite, and short-range aerosol routes?

SARS-CoV-2 transmission is believed to occur primarily through close contact via respiratory droplets produced during talking, coughing or sneezing (CDC 2020a; WHO 2020). Engineering controls implemented to prevent disease transmission during the COVID-19 pandemic include separation (CDC 2020f; OSHA 2020); novel "intubation boxes" to protect healthcare workers from droplet exposure during aerosol generating procedures such as endotracheal intubations and extubations (Chahal et al. 2020; Le et al. 2020); and local exhaust source controls such as the ventilated headboard to protect against droplet and aerosol dissemination (CDC 2020c; Dungi et al. 2015; Mead et al. 2012). With a few exceptions, studies of the effectiveness of intubation boxes and local exhaust source controls are limited, and minimal guidance is available on design dimensions, deployment requirements, and in particular, on the expected performance and limitations of these systems. While the intent of the barriers and intubation boxes is clear, research on how well these devices perform under various workplace conditions is needed to refine designs and improve guidance for local source controls to prevent the spread of SARS-CoV-2 as well as future pathogens of concern.

Another engineering control method that has been proposed to reduce SARS-CoV-2 transmission is ultraviolet germicidal irradiation (UVGI). UVGI has been shown to be effective at inactivating pathogens on surfaces and in the air (Nardell 2016; Weber et al. 2016). However, little is known about the efficacy of UVGI against SARS-CoV-2, including the dose of UVGI required to inactivate the virus and the effects of temperature, humidity, and the presence of other organic material on virus susceptibility to UVGI.

Do transparent barriers between workers and customers reduce exposure to aerosols containing SARS-CoV-2?

Transparent barriers between workers and customers are being widely deployed to reduce the risk of transmission of SARS-CoV-2. However, the effectiveness of this intervention has not been evaluated for the prevention of respiratory infections. Face shields have been shown to substantially reduce exposure to larger aerosol particles from a simulated cough, especially at close range, but the effectiveness of face shields is much less for smaller particles (Lindsley et al. 2014), and similar results might be

expected for transparent barriers. While the volume and size distribution of aerosols generated during a cough, sneeze, or a routine exhalation is highly variable (Gralton et al. 2011), vocalization and normal breathing, in particular, do generate aerosols in the respirable size fraction (Asadi et al. 2019, 2020), and it is reasonable to expect transparent barriers would be less effective against these aerosols. On the other hand, the use of these barriers is likely to reduce the exposure to larger droplets. Transparent barriers also affect the ventilation and airflow in a workspace, which could affect aerosol distribution and subsequent exposure in positive or negative ways. Research is needed on the degree of protection provided by transparent barriers against aerosols containing SARS-CoV-2, and especially the effects of particle size on exposure reduction. Such research could help determine the effectiveness of different types and geometries of transparent barriers at reducing transmission of SARS-CoV-2 to workers and whether additional controls and precautionary measures need to be implemented.

Do ventilation systems contribute to the dissemination and subsequent exposure to aerosols containing SARS-CoV-2?

One of the most common questions about building ventilation systems that are posed to public health organizations and engineering societies is whether HVAC systems can distribute viable SARS-CoV-2-containing aerosols, leading to exposures through surfaces and air. The CDC has stated that airborne transmission of COVID-19 from person-to-person over long distances is unlikely (CDC 2020a). However, SARS-CoV-2 RNA has been found in air samples within patient rooms and on HVAC supply and exhaust grills in restaurants, patient rooms, and patient restrooms (Ding et al. 2020; Liu et al. 2020; Ong et al. 2020). Thus, it is not clear if, for example, low concentrations of viable virus could accumulate in certain locations in an HVAC system.

The lack of information on this topic at the time of national and international return-to-work strategy implementation has both economic and public health planning consequences. Answering this question will require reliable sampling methods for both air and surface sampling, including measurements of culturable virus. This research is time-sensitive and critical to facilitating a knowledge-based return-to-work strategy and to direct COVID-19 intervention efforts and resources effectively.

How contaminated are N95 filtering facepiece respirators (FFRs) that are exposed to SARS-CoV-2 bioaerosols?

With limited FFR availability, healthcare facilities have employed extended use, limited reuse, and decontamination to optimize supplies (CDC 2020e). Self-inoculation from handling contaminated FFRs is a concern when practicing FFR extended use and reuse (Brady et al. 2017). For this reason, FFR decontamination has been adopted by many healthcare facilities. However, decontamination can impair FFR performance, may leave harmful residues on the FFR, and temporarily reduces the number of available FFRs while the devices are being decontaminated (CDC 2020d). Moreover, standard methods to measure FFR decontamination efficacy are lacking. One study assessed SARS-CoV-2 contamination of a small sample of N95 FFRs and reported no detectable virus (Ong et al. 2020). Similarly, other studies have found minimal or no contamination on FFRs and facemasks used while caring for patients with expected and confirmed influenza (Ahrenholz et al. 2018; Rule et al. 2018). The risks associated with the limited reuse of minimally contaminated FFRs may be more acceptable compared to the risks and challenges of FFR decontamination. High levels of FFR contamination may confirm the need for FFR decontamination or the need for devices that afford a higher level of respiratory protection than N95 FFRs. Assessing the level of bioaerosol contamination of used FFRs will provide empirical data to prioritize supply optimization strategies, determine the appropriate level of respiratory protection, and establish decontamination efficiency requirements for a standard method.

Does transmission of SARS-CoV-2 occur by aerosol inoculation of the ocular surface?

SARS-CoV-2 is a highly contagious respiratory virus that has been shown to be infectious in aerosols for up to three hours in a laboratory setting (van Doremalen et al. 2020). Symptomatic, pre-symptomatic and asymptomatic individuals may expel virus-laden particles when coughing, sneezing, talking, or breathing, which may facilitate transmission (Asadi et al. 2020). The epithelium of the human eye is a mucosal surface that may serve as a portal of SARS-CoV-2 transmission (Napoli et al. 2020). Hoffmann et al. (2020) demonstrated that binding of the SARS-CoV-2 surface-bound Spike protein (S) to angiotensin-converting enzyme-2 (ACE2) receptors and cleavage by serine protease TMPRSS2, enables host cellular entry. Because human ACE2 receptors and the TMPRSS2 protein are found in the conjunctiva and cornea, ocular transmission of airborne SARS-CoV-2 is highly plausible (Napoli et al. 2020).

Several reports suggest that unprotected ocular exposure to SARS-CoV-2 droplets may enable viral entry and disease manifestation (Yu et al. 2020a), and current CDC guidelines for healthcare workers include the use of eye protection when treating COVID-19 patents, but the importance and mechanisms of ocular transmission remain unclear. Additional research looking at whether transmission of SARS-CoV-2 can occur by aerosol inoculation of the ocular surface is greatly needed. Such studies would contribute to eye protection recommendations and use in occupational settings.

Which animal model is best suited to study aerosol and droplet transmission of SARS-CoV-2?

Animal models that are permissive to infection and mimic the pathogenesis of SARS-CoV-2 in humans are ideal for assessing the modes of transmission (Callaway 2020; Sutton and Subbarao 2015; Yuan et al. 2020). Key to transmission is the ability of the S protein of SARS-CoV-2 to bind the ACE2 receptor on host cells (Hoffmann et al. 2020; Wrapp et al. 2020). Wan et al. (2020) stated that mice will not be a good model unless they were genetically engineered to express the human ACE2 receptor but that pigs, ferrets, cats, and nonhuman primates may be good animal models because their ACE2 protein sequences are identical or very similar to human ACE2. Recent studies have shown that SARS-CoV-2 can replicate in macaques (Deng et al. 2020; Rockx et al. 2020; Yu et al. 2020b), golden Syrian hamsters (Chan et al. 2020), and ferrets (Shi et al. 2020). Kim et al. (2020) showed that ferrets could indirectly transmit SARS-CoV-2 to naïve ferrets housed in separate cages, which the authors suggest indicates airborne transmission.

Devising experiments that distinguish between transmission by large ballistic droplets and smaller droplets that remain airborne is more challenging than is often appreciated. Determination of the sizes of the virus-laden particles emitted by the infected animal and inhaled by the naïve animal would need to be determined through aerosol sampling. Experiments could be tailored to artificially aerosolize various size ranges of virus-laden particles into a room with animals and study the effects of particle size on disease transmission.

Conclusions

Protecting workers from becoming infected with COVID-19 presents substantial challenges, in part because much remains to be learned about how this disease is spread and how best to prevent it. The list of research questions posed here is not meant to be exhaustive. Rather, it is intended to convey some of the workplace aerosol research topics that need to be addressed with regard to SARS-CoV-2, with the hope that it will inspire fresh ideas and new projects to study these and related questions. The global community of aerosol scientists brings a unique understanding of airborne particle behavior to studies of the transmission of infectious diseases, and the information that will be discovered as these research areas are explored will be critical both during the current pandemic and during future pandemics that inevitably will occur.

Disclosure statement

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

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