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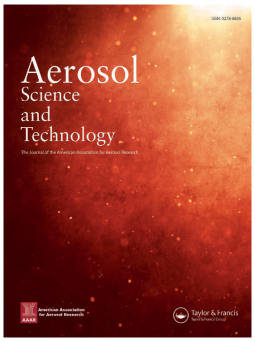

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EDITORIAL

The coronavirus pandemic and aerosols: Does COVID-19 transmit via expiratory particles?

As of late March 2020, the global COVID-19 pandemic caused by the SARS-CoV-2 virus has battered the world. More than 40,000 people have died with over 800,000 people confirmed infected; financial markets have crashed; restaurants and public plazas are deserted; countries have effectively closed their borders; and millions of people are confined to their homes under shelter-in-place orders. Virologists and epidemiologists are racing to understand COVID-19 and how best to treat it. Many unknowns remain, but one thing is eminently clear: COVID-19 is both deadly and highly transmissible.

A mysterious aspect, however, involves *why* it is so transmissible. Here we would like to pose a simple question: what role do aerosols play in transmission of COVID-19?

This question is easy to ask but extremely challenging to answer. When an infected individual reports to a hospital there is no way to assess *definitively how* they were infected. The "contact-tracing" performed by epidemiologists carefully tracks who came into "close contact" with a patient under investigation, but it cannot tell you how the virus itself was transferred from the contagious person to those whom they infected. There is broad agreement in the infectious disease community about possible modes of respiratory virus transmission between humans (Tellier et al. 2019). Direct or indirect "contact" modes require a susceptible individual to physically touch themselves with, for example, a virus-contaminated hand; "direct" indicates that person-to-person contact transfers the virus between infected and susceptible hosts (such as by a handshake), while "indirect" implies transmission via a "fomite," which is an object like a hand-rail or paper tissue that has been contaminated with infectious virus. In contrast, airborne transmission may occur by two distinct modes and requires no physical contact between infected and susceptible individuals. During a sneeze or a cough, "droplet sprays" of virus-laden respiratory tract fluid, typically greater than 5 µm in diameter, impact directly on a susceptible individual. Alternatively, a susceptible person can inhale microscopic aerosol particles consisting of the residual solid components of evaporated respiratory droplets, which are tiny enough (<5 µm) to remain airborne for hours.

It is unclear which of these mechanisms plays a key role in transmission of COVID-19. Much airborne disease research prior to the current pandemic has focused on 'violent' expiratory events like sneezing and coughing (e.g., Lindsley et al. 2013; Bourouiba, Dehandschoewercker, and Bush 2014). There is strong evidence now, however, that many infected individuals who transmit COVID-19 are either minimally symptomatic or not symptomatic at all. In China, Chan et al. (2020), Zou et al. (2020), and Hu et al. (2020) all reported the existence of asymptomatic individuals who tested positive for the SARS-CoV-2, and virus transmissions from asymptomatic carriers have been identified (Rothe et al. 2020). Most recently, epidemiologists led by Shaman et al. (Li et al. 2020) calculated that about 86% of infections in Wuhan, China, prior to the implementation of travel restrictions, were "undocumented" individuals, those with "mild, limited, or no symptoms" who accordingly were never tested. Notably, their modeling indicated that 79% of the actual documented cases were infected by undocumented individuals. Furthermore, inspection of the average delay time between infection and initial manifestation of symptoms led them to conclude that "… pre-symptomatic shedding [of virus] may be typical among documented cases."

In other words, it appears that large numbers of patients who became ill enough to require hospital treatment could have themselves been infected by others who did not appear sick.

Asymptomatic and pre-symptomatic individuals, by definition, do not cough or sneeze to any appreciable extent. This leaves direct or indirect contact modes and aerosol transmission as the main possible modes of transmission. Much media attention has correctly focused on the possibility of direct and indirect transmission via for example contaminated hands, with public health messages focusing on the importance of washing hands thoroughly and often, and of greeting others without shaking hands.

Less attention has focused on aerosol transmission, but there are important reasons to suspect it plays a role in the high transmissibility of COVID-19. Air sampling performed by Booth et al. (2005) established that hospitalized patients infected with SARS during the 2003 epidemic emitted viable aerosolized virus into the air. Notably, that outbreak was caused by SARS-CoV-1, the closest known relative in humans to the SARS-CoV-2 virus responsible for the current pandemic. These viruses are not the same, but recent experimental work by van Doremalen et al. (2020) demonstrated that aerosolized SARS-CoV-2 remains viable in the air with a half-life on the order of 1 h; they concluded that both "…aerosol and fomite transmission of SARS-CoV-2 is plausible, since the virus can remain viable and infectious in aerosols for hours and on surfaces up to days."

Their experimental work involved artificially generated and aged aerosols using a nebulizer and maintaining it suspended in the air with a Goldberg drum. But if pre- or asymptomatic infected individuals do not sneeze or cough, how do they generate aerosols? In fact long ago it was established that ordinary breathing and speech both emit large quantities of aerosol particles (Duguid 1946; Papineni and Rosenthal 1997). These expiratory particles are typically about 1 micron in diameter, and thus invisible to the naked eye; most people unfamiliar with aerosols are completely unaware that they exist. The particles are sufficiently large, however, to carry viruses such as SARS-CoV-2, and they are also in the correct size range to be readily inhaled deep into the respiratory tract of a susceptible individual (Heyder et al. 1986). Recent work on influenza (another viral respiratory disease) has established that viable virus can indeed be emitted from an infected individual by breathing or speaking, without coughing or sneezing (Yan et al. 2018).

Ordinary speech aerosolizes significant quantities of respiratory particles. Experimental work by Morawska et al. (2009) indicated that vocalization emits up to an order of magnitude more aerosol particles than breathing, and recent work by Asadi et al. (2019) established that the louder one speaks, the more aerosol particles are produced. Asadi et al. further established that, for unclear reasons, certain individuals are "speech superemitters" who emit an order of magnitude more aerosol particles than average, about 10 particles/second. A ten-minute conversation with an infected, asymptomatic superemitter talking in a normal volume thus would yield an invisible "cloud" of approximately 6,000 aerosol particles that could potentially be inhaled by the susceptible conversational partner or others in close proximity.

Estimating the actual probability of transmission due to this cloud requires information from two traditionally distinct disciplines: virology and aerosol science. In regard to virology, information is required about the average viral titer in the respiratory fluid and the emitted aerosol particles, as well as the minimum infectious dose for COVID-19 in susceptible individuals. During speech, these particles likely derive in part from a "fluid film burst" mechanism in the alveoli in the lungs as well as via vibration of the vocal cords (Johnson et al. 2011), so the breath and speech derived particles may contain virions if mucus in the respiratory tracts contains them. COVID-19 is a respiratory infection, and early work clearly established the presence of SARS-CoV-2 in the respiratory tract (Zhu et al. 2020). Neither the aerosol viral load nor the minimum infectious dose for COVID-19 have been definitively established, although it is believed for other viral respiratory illnesses that a single virus can serve to initiate infection (Nicas, Nazaroff, and Hubbard 2005).

Even if these details about virus production and infectiousness were known with perfect accuracy, however, it is also necessary to calculate how these particles move through the air to a susceptible individual. This is where transport analysis and aerosol science are paramount. The classic Wells-Riley model of transmission assumes that air in a room is well mixed (Wells 1934; Xie et al. 2007), but exhaled particles (either indoors or outdoors) transport in a puff or plume that travels in the direction of the background air motion (Wei and Li 2016). People close to each other may not transmit due to countervailing background air motion, just as people far apart may transmit if the air motion efficiently transports virus-containing particles from an infected individual to a naïve one. Furthermore, droplets and expiratory particles may settle fast enough by gravity to be removed from the air before being inhaled. Further complicating matters, increased air speeds might serve to transport the expiratory particles further to reach additional susceptible people, or serve to increase turbulence in the air and correspondingly dilute the particle concentration and reduce the chance of infection.

Clearly there are many complicated unknowns, which in general have stymied definitive assessment of the role of aerosols in airborne disease transmission. But given the large numbers of expiratory particles known to be emitted during breathing and speech, and given the clearly high transmissibility of COVID-19, a plausible and important hypothesis is that a face-to-face conversation with an asymptomatic infected individual, even if both individuals take care not to touch, might be adequate to transmit COVID-19.

Note that the key word in the last sentence was "might." Many urgent questions about aerosol transmission and COVID-19 must be answered. Do infected but asymptomatic individuals emit more expiratory aerosols than the healthy individuals tested to date? Do these expiratory aerosols contain virions and how do the viral titers in these aerosols change with time post-infection and post-emission? What are the optimal protocols and techniques for sampling bioaerosols containing SARS-CoV-2 and how do we assess their virulence? How do ambient environmental conditions, such as temperature and humidity, affect airborne virus viability? What animal models are best for simulating airborne human transmission of COVID-19?

Although we argue here that speech plausibly serves as an important and under-recognized transmission mechanism for COVID-19, it is up to aerosol scientists to provide the technology and hard data to either corroborate or reject that hypothesis. In terms of technology, improved bioaerosol sampling technology (Pan et al. 2016) is necessary; in terms of science, closer collaboration between virologists, epidemiologists, and aerosol scientists (Mubareka et al. 2019) is necessary; and in terms of outreach, improved efforts to inform the public that every individual emits potentially infectious aerosols all the time, not just when sneezing or coughing, is necessary.

The stakes for the world are enormous. The aerosol science community needs to step up and tackle the current challenge presented by COVID-19, and also help better prepare us for inevitable future pandemics.

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