PNAS COMMENTARY

Abrupt decreases in infectivity of SARS-CoV-2 in aerosols

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A respiratory virus emitted in an aerosol particle will experience a tough journey with many obstacles before finding a new host where it can cause an infection (Fig. 1). By every second, its chances to replicate decrease due to removal by building ventilation, deposition on surfaces, or loss in infectivity. Thus, the transport of infectious viruses from the exhaled breath of one person to the inhaled air of another typically occurs within a few minutes. During this short time, the aerosol will undergo several transformations because of changing environmental conditions. Nevertheless, due to methodological challenges, we still have a remarkably limited understanding of the relationships between environmental factors and survival of pathogens in aerosols on short timescales. In a study in PNAS, Oswin et al. (1) show that the infectivity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can decrease abruptly when aerosol particles move between environments.

Traditionally, most studies of the viability of viruses in aerosols have used specially designed rotating drums, so-called Goldberg drums, where the particles can be suspended in air for a long time. Such studies have shown that SARS-CoV-2 can remain infectious for hours in aerosols (2, 3). However, the time resolution of these experimental systems is poor, and the environment inside the drums is artificial with its controlled steady-state conditions.

Oswin et al. (1) trapped aerosol droplets containing SARS-CoV-2 in a small volume of air in an electric field where they controlled the environmental conditions with high precision. Thereby, they could measure the virus stability on timescales down to 5 s. Furthermore, a constant airflow around the droplets made it possible to swiftly alter the environmental parameters between, for instance, high relative humidity, where the aerosol particles contain a large fraction of water, and low relative humidity, where some of the solutes crystalize. By these means, they demonstrate an exciting and complex interplay between microphysical processes and virus viability. Contrary to what may be assumed from rotating drum studies, the decay in infectivity of viruses in aerosols is not smooth and gradual. Instead, infectivity can remain relatively stable for a long time when the environment is kept constant but change substantially within minutes, or even seconds, when the aerosol particles are equilibrating to new conditions.

In reality, an airborne virus will encounter dynamic surroundings, and, to be able to estimate the risk of disease transmission through aerosols, we need to understand the transformation processes that are going on (1, 4). Respiratory viruses are emitted during talking, singing, breathing, or coughing (5). Immediately upon exhalation, the viruses experience their first brutal change in conditions. The air inside the respiratory tract is almost saturated with water vapor, the temperature is near 37 °C, and the CO_2 level is up to 4 to 5% by volume. Thus, in most environments where humans dwell, the humidity and temperature will decrease considerably after exhalation, and CO_2 will drop by two orders of magnitude. If the relative humidity falls below around 50%, the salts in the aerosol droplets crystallize, which, according to Oswin et al. (1), can cause an almost immediate loss in infectivity of half of the viruses or more. The effect of the decreasing CO_2 level is more uncertain. The same chemical balance that currently makes the oceans more acidic due to anthropogenic emissions of CO_2 will have the opposite effect on the exhaled aerosol droplets and make them more alkaline. It is, however, unclear whether this increase in pH is sufficient to have a significant effect on the viability for SARS-CoV-2.

Although a major part of the exhaled viruses may lose their infectivity within only a few minutes, this time is sufficient for the aerosol particles to travel many meters in indoor air, where most of the disease transmission occurs. It has been a common misunderstanding that short-range transmission of respiratory disease depends on large droplets that deposit within 1 m to 2 m, while long-range transmission is caused by smaller aerosol particles. However, inhalation of aerosols is a main route of transmission at both short and long ranges. Three factors contribute to a decrease in transmission risk with distance: dilution, loss of infectivity, and deposition on surfaces during transport to a new host. Thus, long-range spread of disease is less common. For any particle size, the concentration of infectious aerosol particles will be higher close to the source than farther away, especially in ventilated spaces (6).

In many ways, the indoor environment is protective for pathogens, with its relatively stable temperature, absence of UV exposure, and moderate variability in humidity. Therefore, the aerosolized viruses that survive the transition from exhaled air can remain viable for comparatively long periods inside a building. If the viruses are inhaled, they will likely experience a sharp increase in humidity and temperature before being deposited in the respiratory tract or exhaled a second time.

Oswin et al. (1) find that, at least on short timescales, low relative humidity is associated with poorer survival for SARS-CoV-2. This can appear contradictory to epidemiological studies that link dry air to increased risk for transmission of

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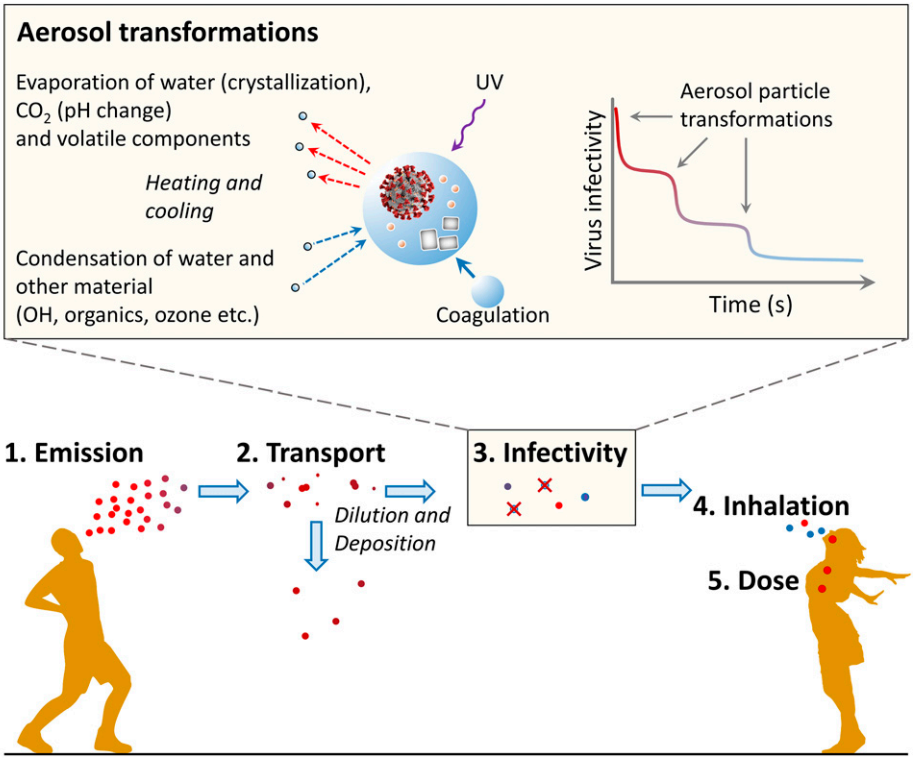

Fig. 1. Transmission of respiratory viruses through aerosols. Viruses may be emitted through coughing and sneezing, but also during talking or just ordinary breathing. During transport, their concentration will decrease with distance, due to dilution and deposition on surfaces, and their infectivity will decline with time. A study in PNAS by Oswin et al. (1) provides insights into how virus infectivity is affected by aerosol microphysics and shows that it can decrease rapidly depending on surrounding environment.

respiratory viruses (7, 8). However, virus viability is only one piece in the puzzle. Dry air will result in a more rapid evaporation of the aerosol droplets, which, in turn, will decrease their size and increase their residence time in air. Furthermore, dry air may weaken mucociliary clearance in the lungs, impair innate antiviral defense, and reduce tissue repair function (9). Together, these factors may very well outweigh the observed lower infectivity at low relative humidity.

Considering all barriers to airborne transmission and the large decline in infectivity during the first minutes, it may seem doubtful that aerosols contribute significantly to the spread of SARS-CoV-2. Therefore, the reported infectivity losses must be related to the amounts of viruses that are released with exhaled air and the dose required to cause an infection. Some individuals emit thousands of viruses every minute at peak viral load (5, 10). In poorly ventilated spaces, these will accumulate, and, even with the infectivity losses up to 90% reported by Oswin et al. (1), a substantial amount will remain viable. Only a few viruses are needed to cause an infection (11). Hence, it is not surprising that inhalation has been identified as a principal way of transmission. There is direct evidence linking SARS-CoV-2 measured in exhaled air of infected persons to observations of increased infection risk among their close contacts (5).

Oswin et al. (1) primarily investigate how SARS-CoV-2 in aerosols is affected by relative humidity, particle crystallization, and droplet pH. Many questions remain. Other environmental factors will also affect viability, such as temperature, radiation, and reactive gas components. The timescales are presumably also dependent on particle size. Oswin et al. used aerosols with a dry size of around 10 μm, and studies with Goldberg drums have focused on 5-μm particles. However, exhaled viruses can be expected in the whole aerosol particle size range of from <0.3 μm to 100 μm (12). Over this range, the droplet evaporation times shift by several orders of magnitude. Additionally, many studies, including the one by Oswin et al., use virus media representative for saliva, but viruses are also emitted from the lower airways and, in particular, the vocal cords. Thus, similar studies with media simulating lung-lining fluid, especially at the larynx, would also be needed. Finally, we still do not know why the viruses lose their infectivity. Is it because of damage on the surface molecules or on the genetic material inside the capsid? And by what mechanism does it happen?

With an improved understanding of the factors that determine the viability of airborne viruses, we have better chances to predict the capability of new viruses and their variants to spread through aerosols. Experimental systems with an ability to examine virus infectivity at short timescales with high environmental control, such as the one used by Oswin et al. (1), can facilitate a more comprehensive understanding of the processes. Their study in PNAS beautifully demonstrates that the infectivity of airborne SARS-CoV-2 can decrease abruptly when exposed to changing environmental conditions and that aerosol microphysics is a key to understand the process.

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