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Clean air in the context of pathogen circulation	*26 May 2023*
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Clean air in the context of pathogen circulation

1 Initial situation

The aim of this document is to emphasise that the considerations regarding the benefit of clean air in the acute phase of the COVID-19 pandemic remain valid in the post-acute phase, as well as for other airborne diseases. We discuss the substantial health benefits that ventilation and air filtration in buildings offer individuals. In the context of infectious diseases, good ventilation of indoor air is generally expected to lead to a reduced pathogen burden. We further discuss challenges and uncertainties related to quantifying the impact of clean air measures on transmission, ensuring clean air while offering a comfortable environment for the people inside the buildings in question, as well as being energy-efficient, and characterising the potential risks of certain proposed clean air measures.

Having clean air inside buildings impacts health as well as overall human well-being, work performance and learning (link, link). As a consequence, clean air may also have relevant economic implications (link). “Clean air” refers to “air that is not polluted”. The WHO defines this as follows: “Air pollution is contamination of the indoor or outdoor environment by any chemical, physical or biological agent that modifies the natural characteristics of the atmosphere” (link).

The WHO points towards indoor air pollution as being an important factor for various diseases, such as cardiovascular and, in particular, respiratory diseases (link, link, link). In the context of infectious diseases, clean air – referring to air without pathogen-laden aerosols – can reduce airborne transmission. This is not a new insight. However, its importance has been highlighted throughout the pandemic. The importance of ventilation to ensure clean air and, in turn, to reduce the burden of a pathogen have been highlighted by the WHO as well as authorities and organizations in Switzerland and abroad in the context of SARS-CoV-2 (link, link, link, link, link, link).

We briefly summarise the main aspects of airborne transmission via pathogen-laden aerosols (Section 2) and possible measures to reduce the amount of pathogen-laden aerosols in the air (Section 3).

2 Current state of scientific knowledge

2.1 Aerosol transmission and clean air

Respiratory pathogens are transmitted (i) over short ranges (in exposure modelling, this is also referred to as the “near field”) through droplets and aerosol particles during close interactions and (ii) over long ranges through aerosol particles carried into and accumulating in the “far field” (see also link for a discussion of droplet sizes and transmission modes in the context of SARS-CoV-2). We note that fomite transmission is a third transmission pathway. However, we will not discuss this further as we are focusing on airborne transmission in this paper.

Transmission is more likely when people are near to each other, as opposed to being further away: droplet exposure only occurs when people are in close proximity. Aerosol concentrations are higher directly to the source and diminish with distance (link). Furthermore, there is an indication that larger particle sizes have higher virus loads (link, link) and that it is most likely that a cloud of different particle sizes at high concentrations exposes an individual to the highest risk of infection. However, long-range transmission might have a particularly relevant impact in large, poorly ventilated rooms with high occupancy: while few people in such settings face the risk of short-range transmission from close neighbours, there are substantially more people at large distances from each other, meaning that many people are exposed to pathogen-laden aerosols. When considering the risk of transmission, all indoor spaces should be taken into account where people spend time together or in succession, i.e. also corridors, toilets, etc. In addition to the level of aerosol concentration, the duration of the stay also influences the resulting dose.

The risks of short-range transmission can be lowered by keeping a distance from others as well as by wearing a medical mask or high-efficiency filtering facepiece (FFP2) (see e.g., link). Masks and FFP2s (without a valve) work both by preventing droplets from being exhaled (source control) and by stopping droplets or aerosols from being inhaled (infection control). FFP2s are superior at preventing inhalation. However, if everyone were using a medical mask, it would protect a person at risk more efficiently than if only this person were wearing an FFP2 and nobody else were wearing a mask or FFP2 (link). Short-range transmission may be lowered further by personal ventilation systems, provided the rooms have a fixed seating arrangement.

Aerosol transmission over long ranges can be reduced by improving air quality with "clean air" measures. In this approach, manual (or natural) ventilation (informed by CO_2 sensors) or mechanical ventilation dilutes the air and transports away pathogen-laden aerosols, while air filtration removes aerosols from the passing airstream and disinfection kills or inactivates the pathogens in aerosols. New concepts in building construction are envisioned (link) to employ these measures to reduce the concentration of pathogen-laden aerosols, while being energy-efficient and providing a comfortable environment for the people inside the building.

"Clean air" measures to improve air quality are expected to have the greatest impact on preventing long-range transmission. Away from the source, the pathogens are more diluted, meaning that a smaller reduction in pathogens is needed to bring airborne concentrations below the minimum infectious dose, compared to short-range exposure. In addition, the time it takes a pathogen to reach the far field allows air purification and disinfection methods to be more effective. The impact also depends on the pathogen emission rate, which defines how high pathogen levels can rise for a given room and ventilation setting and thus how significant additional clean air measures need to be.

The extent of the overall reduction in airborne transmission through clean air measures depends on the importance of long-range transmission for the pathogen in question (compared to short-range transmission), which, in turn, depends on the minimum infectious dose, the pathogen's ability to survive in different particle sizes over time and the proximity of people, among other factors.

Medical masks and, more so, FFP2s can also reduce the concentration of pathogen-laden aerosols over long ranges by preventing the droplets that form aerosols from being exhaled (source control) and by stopping aerosols from being inhaled (infection control). Thus, these measures are effective against both short- and long-range transmission.

Importantly, as transmission occurs on different occasions and through different modes, a "Swiss cheese model'' (link) is typically required to contain spread by interrupting the path of pathogens from an infected person to a healthy person, with clean air measures providing one layer of protection.

3 Possible courses of action

Ways to reduce the concentration of pathogen-laden aerosols in the air encompass (i) preventing the release and inhalation of aerosols, (ii) ensuring air exchange to dilute and eliminate pathogen-laden aerosols, (iii) removing these aerosols with filters, (iv) deactivating the pathogens by disinfecting the air, and (v) potentially modulating pH in indoor air. Approach (i) can be achieved with masks. Its impact as well as consequences have been discussed in other documents such as link and will not be explored further here. In this paper, we are focusing on "clean air" measures (ii-v). We discuss the impact of potential "clean air" measures on transmission and end the section with questions that remain unanswered, followed by risks and benefits other than reducing transmission; see also, e.g., link for details on possible measures.

3.1 Ventilation

Air exchange will dilute aerosol concentrations within a specific space and over time. Air exchange can be achieved through manual or mechanical ventilation. At identical air change

rates per hour, constant mechanical ventilation usually yields lower concentrations because of the build-up during non-ventilated phases.
An association between reduction in incidence of infection/occurrence of transmission and increased ventilation has been observed in the following instances:

- An observational study that showed a reduction in the incidence of tuberculosis with improved ventilation (link).
- A study in a hospital found that "tuberculin conversion among health care workers was strongly associated with inadequate ventilation in general patient rooms and with type and duration of work, but not with ventilation of respiratory isolation rooms" (link).
- For SARS-CoV-2, a study in Italy found that "for classrooms equipped with mechanical ventilation systems, the relative risk of infection of students decreased at least by 74% compared with a classroom with only natural ventilation […]" (link).
- Again for SARS-CoV-2, different attack rates in two buses may be explained by ventilation (link).
- A reduction in influenza transmission in a computational study (link);
- An influenza outbreak on an aeroplane where the ventilation system was not operating (link);
- Good ventilation in wards with isolated SARS cases could reduce the viral load of the ward and reduce the number of healthcare personnel infected (link) (more on SARS link, link, link).

Air exchange can also alter the relative humidity of the indoor air, in particular during the colder months. Specifically, when cold outdoor air enters a room in winter without being re-humidified and is then heated to room temperature, this leads to low relative humidity levels indoors. This has been reported to favour pathogen survival (link, link) and influenza virus transmission (link). In addition, the dehydration of mucosa at low relative humidity may reduce immune response and hence provide favourable conditions for infection with influenza virus (link), at least in mice. Above all, it may be the decrease in humidity (rather than absolute values) that makes the mucosa more susceptible to infection (link). Mechanical ventilation systems with heat recovery and moisture retransfer counteract this. However, the air humidity must not be too high, otherwise there is a risk of respiratory diseases caused by bacteria and mold growth (link, link, link, link).

Conversely, outdoor air can carry volatile acids (e.g., nitric acid), which, when mixed into indoor air, acidify the pathogen-laden aerosol particles. This process will reduce the persistence of some acid-sensitive pathogens (e.g., influenza virus), though it may also cause immune-modulatory effects that increase the occupants' susceptibility to airborne viruses.

Ventilation can be guided with CO_2 sensors to support elevated ventilation rates during periods of high occupancy density and to conserve energy during periods of low or no occupancy. The air change rate needs to be high relative to the virus inactivation rate in the aerosol particles. If the airborne pathogen has, say, a half-life of 60 min (which has been reported for SARS-CoV-2, link), four air exchanges per hour (ACH) would make a clear difference, while 0.2 ACH would have no meaningful effect. Note that four ACH are typically only achieved through mechanical ventilation. Increasing air flow is most effective in poorly ventilated spaces. In rooms that are already well-ventilated, disproportionately large increases in air flow are needed for a similar effect to be achieved (link, link, link, link), with the associated increases in energy consumption also being disproportionately large. The challenge is to determine an optimum trade-off between infection risk and energy use. Further, it remains to be investigated how a person can avoid air flows which put them at an elevated risk of infection (link, link).

Manual (or natural) ventilation is undertaken by opening windows. CO_2 sensors are a relatively cheap way (< CHF 100 per sensor) to ensure that windows are opened often enough, while also preventing windows from being opened too much, and, by extension, stopping excessive amounts of energy from being lost (link). Importantly, while these sensors can serve as a valuable guide, some points need to be borne in mind when using them. First, sensors measure CO_2 concentrations but not the concentration of airborne pathogens or aerosols. The pathogen-laden aerosol concentration is not affected by the number of non-infected people in the room but only by the number of those infected. Secondly, while in many settings, CO_2 and exhaled aerosol concentrations are mostly tightly correlated (see e.g., link), there may be occasions where the CO_2 sensors do not accurately reflect aerosol concentrations, for example, if there is additional air filtration or there is increased aerosol release during singing. Furthermore, the optimum ventilation frequency depends on the lifespan of the infectious virus in the air (see e.g., link). All this leads to uncertainty regarding the best ventilation regime.

Mechanical ventilation can optimise the ventilation of a room and the air flow. Mechanical ventilation can be undertaken using mobile systems or a ventilation system integrated into the building. See also link, link and link. There are two predominant mechanical ventilation concepts, namely "ventilation by displacement" and "ventilation by mixing". In displacement ventilation, there is no uniform mixing, but directional airflow: usually the air is directed to the floor, rises to the ceiling in the case of heat sources such as people, and is discharged there.

While displacement ventilation should work better in ideal situations (little movement, little speaking, no thermal differences in the room), mixing ventilation is often encouraged in real-world settings (link).

Personalised ventilation is a new development in ventilation systems. This system reduces exposure to pathogen-laden aerosols substantially better than the commonly used forms of mixing or displacement ventilation (link, link) Nevertheless, practical limitations include the fact that it has to be used with fixed seating arrangements as the system cannot adapt to variable room arrangements or changes in layout. Besides this, it requires increased duct work which, depending on installation, can be aesthetically challenging and can increase installation and maintenance costs.

3.2 Air filters

Air filters can reduce aerosol concentrations in enclosed rooms (link, link). As shown in experimental studies, air filters can, in particular, reduce the concentration of SARS-CoV-2 RNA in patient settings (link, link), in a community settings (link, link) and in a Swiss school (link). Furthermore, they may reduce the infection risk on aeroplanes (link). Several modelling studies suggest that the transmission of SARS-CoV-2 was reduced by air filters (link). However, no real-life study has been able to clearly prove or disprove the direct effect of air filters on the human-to-human transmission of SARS-CoV-2 or other respiratory viruses (link) (a Swiss study aiming to evaluate their effect is not conclusive in our view, link). Above all, this lack of a clear result is due to substantial methodological challenges in real-life studies. Some studies only assessed the presence or absence of an air filtering device. However, it is also important to assess whether the devices are running, at what level and with what type of filter. Essentially, while air filters reduce the amount of aerosols in enclosed settings, it remains unclear to what extent ventilation in non-enclosed settings makes air filters redundant (link) (the correct placement and dimension required for a beneficial outcome is not always obvious, link).

3.3 Ultraviolet light

Ultraviolet (UV) light can be used as a disinfectant to destroy airborne and surface-bound pathogens, see e.g., link, section 4.10 and link. Most UV frequencies are harmful to human skin and eyes. Consequently, they are used either in closed systems or for upper-room UV germicidal irradiation (link, link). Far UV light in the range of 200 to 220 nm seems to be an exception as it has been suggested that this is safe for human skin and eyes at highly effective germicidal intensities (link, link, link, link, link, link, link, link). However, in the presence of volatile air pollutants that are frequently found indoors, UV light can contribute to the formation of particulates and other secondary air pollutants which may have detrimental effects on humans (link) in insufficiently ventilated rooms. Research is being performed to understand the effects better (see e.g., link). It also remains unknown whether respecting minimum ventilation rates could be sufficient to control such secondary risks of air disinfection methods.

3.4 pH modulation

Research is currently underway to determine whether **modulating the pH of indoor air** is another way to improve air quality. Acids and bases influence indoor air quality (link). However, it is unclear how pH should be regulated to generate a positive effect. Acid-forming gases lower the pH of aerosols. One study suggests that this can reduce the lifespan of some bacterial and viral pathogens in the air (link); another study concludes that lowering pH extends lifespan (link). However, these gases are also air pollutants that have been shown to reduce host immunity and increase the risk of infection (link, link). There is uncertainty about the optimal range for the possible use of acidifying gases as disinfectants. Further, it is unclear whether clean indoor air measures discussed above significantly change the pH of the air.

3.5 Summary

Ventilation
Ventilation is associated with a decrease in indoor transmission. This association has been seen across many studies and suggests a causative effect, though quantifying this effect poses a challenge. The effect of ventilation on transmission may be especially pronounced for pathogens with indoor superspreading potential, such as SARS-CoV-2. Ventilation can therefore be an important tool in the fight against airborne infections.

Maintaining adequate ventilation is important not only for reducing airborne infection risk, but also for overall human well-being, work performance and learning (link, link), with clear economic implications (link).

With increased ventilation without moisture recovery, the inflow of cold air during the winter months does, however, decrease relative humidity. In turn, this makes the mucosa more susceptible to infection, meaning that ventilation may need to go hand-in-hand with humidification. Ventilation without heat recovery can be energy-consuming, requiring additional heating.

Air filters

While plausible concepts and laboratory as well as field studies show that air filtration reduces the amount of airborne pathogens, there are no conclusive epidemiological studies on its impact on human-to-human transmission. However, air filters have major health benefits in general, removing pollen and other pollutants from the air.

UV disinfectants

For UV disinfectants, the uncertainty as to their impact on transmission is similar to the situation with air filters. It is important to note that UV disinfectants may increase the number of nanoparticles and organic gases in the air, with unknown health implications for humans. These potential risks are not well-understood. It is not clear to what extent aspects such as the placement of the system, intensity setting and accompanying measures need to be fine-tuned so that the desired output is achieved while keeping the risks under control.

pH modulation

The relevance and impact of controlling pH is not understood well enough at this point for it to be used as a clean air measure.