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Opinion Paper

Review of the efficacy of HEPA filtered air to control coronavirus risks in cleanrooms

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Introduction

The risk of viral transmission in the built environment is a matter of concern in the era of the novel coronavirus pandemic, for most of society, given that humans spent the majority of their time indoors. For pharmaceuticals and healthcare, there is an additional concern about working in cleanrooms and the degree to which protective measures are appropriate. With cleanrooms, an important concern is with the efficacy of HEPA filters. This article looks at the risks stemming from SARS-CoV-2 and applies these to the cleanroom context. The article concludes that the cleanroom environment does not contribute to the risk of viral transmission, and certain design aspects can, in fact, reduce the risk compared with other built environments.

Characteristics of the novel coronavirus

Coronaviruses (CoV) are a large family of viruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and SARS-CoV). Coronaviruses are zoonotic, meaning they can be transmitted between animals and people [1]. Coronaviruses are classified as RNA ‘enveloped’ viruses, whereas viruses such as rotavirus, or poliovirus are termed non-enveloped. Enveloped viruses have an envelope or outer coating which is needed by the virus to help it attach to the host cell. If this outer coating is destroyed, for example by a disinfectant, the virus cannot survive. The mode of transmission for enveloped viruses is characterized by the specific virus; however, the most common routes are via indirect or direct contact of infectious virus particles, contact with or inhalation of respiratory droplets [2].

The specific coronavirus of concern is SARS-CoV-2, with SARS standing for ‘severe acute respiratory syndrome’ and CoV representing ‘coronavirus’. The associated respiratory disease is termed COVID-19 (to represent ‘coronavirus disease 2019). This particular virus can cause severe respiratory disease because cells in the lung are damaged and no longer able to transport oxygen into the bloodstream. Some symptoms of disease such as fever and fatigue result from the activities of the immune system trying to eliminate the infection from the body. Heat (fever) inactivates viruses and fatigue results from the high energy demands of the immune system fighting the virus [3].

General cleanroom considerations

Important considerations for cleanroom operators include the behaviour of operators, such as whether they are effectively washing their hands-on entry into the facility and then practicing hand sanitisation as part of the gowning process. In relation to the risk of contracting COVID-19, maintaining social distancing where possible is an additional behavioural activity of importance. Cleaning and disinfection needs to be extended within the facility to fomites (objects or materials that are likely to carry infectious diseases).

Virus transmission, air supply and control

An additional concern for cleanroom managers is with understanding the spatial dynamics and building operational factors that could potentially promote or mitigate the spread and transmission of COVID-19. A standard building provides a greater risk of viral transmission compared to the outdoor environment, mediated through the relative ease of viral exchange and transfer through the air [3]. An important factor is with the occupant density in buildings, as well as the building type and indoor activity, in terms of the risk of accrual of human-associated microorganisms [4]. It follows that the higher the occupant density and the greater the level of indoor activity level, then the higher the level of social interaction and connectivity, and hence the higher the chance of contracting the virus.

With SARS-CoV-2 this is apparent from the initial studies in relation to hospitals in Wuhan, China, from December 2019, and the quarantined cruise ship the Diamond Princess, in January 2020 [5]. Data relates to the 'R0' value (the basic reproduction number of the virus, which provides an indication of the average number of people who will contract a disease from one contagious person [6]. Current data suggests a high transmissibility for COVID-19.

In terms of specific risk factors, viral particles pose a risk to operators through being directly deposited and resuspended due as a result natural airflow patterns (or, in the case of most cleanrooms, mechanical airflow patterns). In addition, other triggers of air turbulence like foot fall, walking, and thermal plumes from human bodies can also affect the movement of viral particles indoors [7]. Those infected with COVID-19 can shed viral particles before, during, and after developing symptoms. While viral particles can enter directly through the nose, mouth or eyes, resuspended viral particles can also settle onto fomites. The risk here is when a person makes contact with a surface, there is an exchange particle, and this can include the transfer of viruses from the individual to the surface and vice versa [8].

Air filtration

The SARS-CoV-2 virus can be spread through droplets and spread through aerosolization remains a secondary transmission method (compared with the primary methods of sneezing, coughing and surface transmission). The degree to which mitigation of viral transmission is achieved through air delivery systems is dependent upon inline filtration media. A typical office will have a minimum efficiency reporting value (MERV) of 8. At this level, 70 to 85% of particles ranging from 3.0 to 10.0 µm can be captured [9]. This is insufficient to contain the virus.

Cleanrooms are designed with more stringent minimum filtration efficiency, having a MERV of 7 or greater is required for the pre-filter (which is positioned ahead of heating and cooling equipment). Typically, pre-filters rated MERV-13 or higher are used (which carry the potential to exclude particles ranging from 0.3 to 10.0 µm). This is followed by a high-efficiency particulate air (HEPA) filter, located downstream of cooling coils and fans. A typical cleanroom HEPA filter will remove 99.97% of particles at 0.3 µm in size (described as the most penetrating particle size) [10].

While such filter systems are effective at preventing bacteria and microbial carrying particles from entering the cleanroom space, most viruses, including CoVs, range from 0.004 to 1.0 µm. While this might suggest that HEPA filtration has limited capacity for viral exclusion, in practice, like bacteria, few viruses are observed as individual particles. Most of the viruses expelled from the body are found combined with water, proteins, salts, and other components as large droplets and aerosols. This applies equally to SARS-CoV-2 in the form of aerosolized particles, which are found in a spectrum of sizes, typically 0.25 to 0.5 µm [11]. This indicates that HEPA filters play an important role in virus exclusion and hence lowering the transmission potential of SARS-CoV-2 within the pharmaceutical and healthcare setting. One area of potential weakness relates to any gaps in the edges of filters which could result in a failure to remove pathogens from the shared air environment; such weaknesses should be detectable through properly executed HEPA filter integrity testing.

Air changes and humidity control

Within the cleanroom there are faster air exchange rates in contrast to office areas. Air change rates are designed to remove particles from cleanrooms at a relatively rapid rate (in the context of most cleanrooms having air change rates above 15 air changes per hour, evidence suggests lower transmission of viral infections under conditions of 20 air changes per hour). Furthermore, a 2018 study relating to the coronavirus MERS, in relation to air change rates, found that air change rates at 17 to 20 helped to reduce viral infection [12] by exhausting a higher ratio of indoor air and any airborne viral particles present [13]. Infection has also been shown to be reduced where there is temperature and relative humidity control (humidity above 50%) [14]. Humidity adversely affects coronaviruses through causing interactions with the polar membrane heads that lead to conformational changes of the membrane, in turn this triggers disruption and inactivation of the virus. To assess the impact of indoor ventilation or humidity upon the viral load from air, virologists use bio samplers of the appropriate aerosolization efficiency. The type of lighting can also reduce the half-life of coronaviruses, under conditions of sunlight (although not applicable to most cleanrooms) and ultraviolet light (where germicidal lamps, such as 254-nm UV C, can be fitted in areas like changing rooms) [15].

Other mitigating factors

Given that surfaces can potentially be contaminated with SARS-CoV-2 particles from infected individuals and the settling of aerosolized viral particles and large droplets spread via talking, sneezing, coughing, then other measures need to be assessed. In relation to these risks, the virus survives longest at a relative humidity of 40 percent on plastic surfaces (with a half-life median of around 16 hours) and shortest in aerosol form (a half-life median of just under 3 hours) [16]. Such other factors mitigating the transfer of viral particles in the cleanroom include the wearing of clean (often sterile) garments, face masks, and gloves (which are subject to regular sanitisation).

Summary

This article does not (and cannot) assert that working in cleanrooms protects cleanroom operators from virus like SARS-CoV-2. However, working within a cleanroom does not increase the risk of viral transmission. Given that viruses are commonly associated with larger particles (forming complexes with water, proteins, salts, and so on) in a range of sizes, most of which cannot penetrate high efficiency filters, the risk of ingress into cleanrooms is low. Within the cleanroom, protective measures include personnel behaviours and gowning, coupled with frequent glove sanitisation. Furthermore, ventilation, in terms of higher air exchange rates, is also important in reducing the transmission potential of SARS-CoV-2.

References

1. Wei, Wang W, Zhao X, Zai J, Li X. (2020) Homologous recombination within the spike glycoprotein of the newly identified coronavirus 2019-nCoV may boost cross-species transmission from snake to human, Journal of Medical Virology, 92(4):433-440
2. Luan RS, Wang X, Sun X, et al (2020) Epidemiology, Treatment, and Epidemic Prevention and Control of the Coronavirus Disease 2019: a Review, Sichuan Da Xue Bao Yi Xue Ban.;51(2):131-138
3. Franchini M, Farrugia A, Velati C et al (2020) The impact of the SARS-CoV-2 outbreak on the safety and availability of blood transfusions in Italy, Vox Sang. doi: 10.1111/vox.12928. [Epub ahead of print]
4. Horve PF, Lloyd S, Mhuireach GA, Dietz L, Fretz M, MacCrone G, Van Den Wymelenberg K, Ishaq SL. 2020. Building upon current knowledge and techniques of indoor microbiology to construct the next era of theory into microorganisms, health, and the built environment. J Expo Sci Environ Epidemiol 30:219–217. doi:10.1038/s41370-019-0157-y
5. Mizumoto K, Chowell G. (2020) Transmission potential of the novel coronavirus (COVID-19) onboard the Diamond Princess Cruises Ship, 2020. Infect Dis Model 5:264–270. doi:10.1016/j.idm.2020.02.003
6. Poon LLM, Peiris M. (2020). Emergence of a novel human coronavirus threatening human health. Nat Med 26:317–319. doi:10.1038/s41591
7. Ong SWX, Tan YK, Chia PY, Lee TH, Ng OT, Wong MSY, Marimuthu K. (2020). Air, surface environmental, and personal protective equipment contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a symptomatic patient. JAMA doi:10.1001/jama.2020.3227
8. Vandegrift R, Fahimipour AK, Muscarella M, Bateman AC, Van Den Wymelenberg K, Bohannan B. (2019) Moving microbes: the dynamics of transient microbial residence on human skin. bioRxiv doi:10.1101/586008
9. Institute of Environmental Sciences and Technology. 2016. HEPA and ULPA Filters (IEST-RP-CC001.6). Institute of Environmental Sciences and Technology, Schaumburg, IL
10. Goldsmith CS, Tatti KM, Ksiazek TG, Rollin PE, Comer JA, Lee WW, Rota PA, Bankamp B, Bellini WJ, Zaki SR. 2004. Ultrastructural characterization of SARS coronavirus. Emerg Infect Dis 10:320–326. doi:10.3201/eid1002.030913
11. Liu Y, Ning Z, Chen Y, Guo M, Liu Y, Gali NK, Sun L, Duan Y, Cai J, Westerdahl D, Liu X, Ho K-F, Kan H, Fu Q, Lan K. 2020. Aerodynamic characteristics and RNA concentration of SARS-CoV-2 aerosol in Wuhan hospitals during COVID-19 outbreak. bioRxiv doi:10.1101/2020.03.08.982637
12. Sung M1, Jo S2, Lee SE et al (2018) Airflow as a Possible Transmission Route of Middle East Respiratory Syndrome at an Initial Outbreak Hospital in Korea, Int J Environ Res Public Health. 6;15: 12
13. Wang, J. and Tang, K. Feng, K. and Weifeng,L. (2020) High Temperature and High Humidity Reduce the Transmission of COVID-19 (2020). At: https://ssrn.com/abstract=3551767
14. Qian H, Zheng X. 2018. Ventilation control for airborne transmission of human exhaled bio-aerosols in buildings. J Thorac Dis 10:S2295–S2304. doi:10.21037/jtd.2018.01.24
15. Rutala WA, Weber DJ (2017) Healthcare Infection Control Practices Advisory Committee (HIPAC). Guideline for disinfection and sterilization in healthcare facilities, 2017. Centers for Disease Control and Prevention, Atlanta, GA
16. van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, Tamin A, Harcourt JL, Thornburg NJ, Gerber SI, Lloyd-Smith JO, de Wit E, Munster VJ. (2020) Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. N Engl J Med doi:10.1056/NEJMc2004973

