Ten scientific reasons in support of airborne transmission of SARS-CoV-2

Heneghan and colleagues' systematic review, funded by WHO, published in March, 2021, as a preprint, states: "The lack of recoverable viral culture samples of SARS-CoV-2 prevents firm conclusions to be drawn about airborne transmission".[1] This conclusion, and the wide circulation of the review's findings, is concerning because of the public health implications.

If an infectious virus spreads predominantly through large respiratory droplets that fall quickly, the key control measures are reducing direct contact, cleaning surfaces, physical barriers, physical distancing, use of masks within droplet distance, respiratory hygiene, and wearing high-grade protection only for so-called aerosol-generating health-care procedures. Such policies need not distinguish between indoors and outdoors, since a gravity-driven mechanism for transmission would be similar for both settings. But if an infectious virus is mainly airborne, an individual could potentially be infected when they inhale aerosols produced when an infected person exhales, speaks, shouts, sings, sneezes, or coughs. Reducing airborne transmission of virus requires measures to avoid inhalation of infectious aerosols, including ventilation, air filtration, reducing crowding and time spent indoors, use of masks whenever indoors, attention to mask quality and fit, and higher-grade protection for health-care staff and front-line workers.[2] Airborne transmission of respiratory viruses is difficult to demonstrate directly.[3] Mixed findings from studies that seek to detect viable pathogen in air are therefore insufficient grounds for concluding that a pathogen is not airborne if the totality of scientific evidence indicates otherwise. Decades of painstaking research, which did not include capturing live pathogens in the air, showed that diseases once considered to be spread by droplets are airborne.[4] Ten streams of evidence collectively support the hypothesis that SARS-CoV-2 is transmitted primarily by the airborne route.[5]

First, superspreading events account for substantial SARS-CoV-2 transmission; indeed, such events may be the pandemic's primary drivers.[6] Detailed analyses of human behaviours and interactions, room sizes, ventilation, and other variables in choir concerts, cruise ships, slaughterhouses, care homes, and correctional facilities, among other settings, have shown patterns—eg, long-range transmission and overdispersion of the basic reproduction number (R_0), discussed below—consistent with airborne spread of SARS-CoV-2 that cannot be adequately explained by droplets or fomites.[6] The high incidence of such events strongly suggests the dominance of aerosol transmission.

Second, long-range transmission of SARS-CoV-2 between people in adjacent rooms but never in each other's presence has been documented in quarantine hotels.[7] Historically, it was possible to prove long-range transmission only in the complete absence of community transmission.[4]

Third, asymptomatic or presymptomatic transmission of SARS-CoV-2 from people who are not coughing or sneezing is likely to account for at least a third, and perhaps up to 59%, of all transmission globally and is a key way SARS-CoV-2 has spread around the world,[8] supportive of a predominantly airborne mode of transmission. Direct measurements show that speaking produces thousands of aerosol particles and few large droplets,[9] which supports the airborne route.

Fourth, transmission of SARS-CoV-2 is higher indoors than outdoors[10] and is substantially reduced by indoor ventilation.[5] Both observations support a predominantly airborne route of transmission.

Fifth, nosocomial infections have been documented in health-care organisations, where there have been strict contact-and-droplet precautions and use of personal protective equipment (PPE) designed to protect against droplet but not aerosol exposure.[11]

Sixth, viable SARS-CoV-2 has been detected in the air. In laboratory experiments, SARS-CoV-2 stayed infectious in the air for up to 3 h with a half-life of 1·1 h.[12] Viable SARS-CoV-2 was identified in air samples from rooms occupied by COVID-19 patients in the absence of aerosol-generating health-care procedures[13] and in air samples from an infected person's car.[14] Although other studies have failed to capture viable SARS-CoV-2 in air samples, this is to be expected. Sampling of airborne virus is technically challenging for several reasons, including limited effectiveness of some sampling methods for collecting fine particles, viral dehydration during collection, viral damage due to impact forces (leading

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to loss of viability), reaerosolisation of virus during collection, and viral retention in the sampling equipment.[3] Measles and tuberculosis, two primarily airborne diseases, have never been cultivated from room air.[15]

Seventh, SARS-CoV-2 has been identified in air filters and building ducts in hospitals with COVID-19 patients; such locations could be reached only by aerosols.[16]

Eighth, studies involving infected caged animals that were connected to separately caged uninfected animals via an air duct have shown transmission of SARS-CoV-2 that can be adequately explained only by aerosols.[17]

Ninth, no study to our knowledge has provided strong or consistent evidence to refute the hypothesis of airborne SARS-CoV-2 transmission. Some people have avoided SARS-CoV-2 infection when they have shared air with infected people, but this situation could be explained by a combination of factors, including variation in the amount of viral shedding between infectious individuals by several orders of magnitude and different environmental (especially ventilation) conditions.[18] Individual and environmental variation means that a minority of primary cases (notably, individuals shedding high levels of virus in indoor, crowded settings with poor ventilation) account for a majority of secondary infections, which is supported by high-quality contact tracing data from several countries.[19,20] Wide variation in respiratory viral load of SARS-CoV-2 counters arguments that SARS-CoV-2 cannot be airborne because the virus has a lower R_0 (estimated at around 2·5)[21] than measles (estimated at around 15),[22] especially since R_0, which is an average, does not account for the fact that only a minority of infectious individuals shed high amounts of virus. Overdispersion of R_0 is well documented in COVID-19.[23]

Tenth, there is limited evidence to support other dominant routes of transmission—ie, respiratory droplet or fomite.[9,24] Ease of infection between people in close proximity to each other has been cited as proof of respiratory droplet transmission of SARS-CoV-2. However, close-proximity transmission in most cases along with distant infection for a few when sharing air is more likely to be explained by dilution of exhaled aerosols with distance from an infected person.[9] The flawed assumption that transmission through close proximity implies large respiratory droplets or fomites was historically used for decades to deny the airborne transmission of tuberculosis and measles.[15,25] This became medical dogma, ignoring direct measurements of aerosols and droplets which reveal flaws such as the overwhelming number of aerosols produced in respiratory activities and the arbitrary boundary in particle size of 5 μm between aerosols and droplets, instead of the correct boundary of 100 μm.[15,25] It is sometimes argued that since respiratory droplets are larger than aerosols, they must contain more viruses. However, in diseases where pathogen concentrations have been quantified by particle size, smaller aerosols showed higher pathogen concentrations than droplets when both were measured.[15]

In conclusion, we propose that it is a scientific error to use lack of direct evidence of SARS-CoV-2 in some air samples to cast doubt on airborne transmission while overlooking the quality and strength of the overall evidence base. There is consistent, strong evidence that SARS-CoV-2 spreads by airborne transmission. Although other routes can contribute, we believe that the airborne route is likely to be dominant. The public health community should act accordingly and without further delay.

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1 Heneghan C, Spencer E, Brassey J, et al. SARS-CoV-2 and the role of airborne transmission: a systematic review. *F1000Research* 2021; published online March 24. https://doi.org/10.12688/f1000research.52091.1 (preprint).
2 Prather KA, Wang CC, Schooley RT. Reducing transmission of SARS-CoV-2. *Science* 2020; **6498:** 1422–24.
3 Pan M, Lednicky JA, Wu CY. Collection, particle sizing and detection of airborne viruses. *J Appl Microbiol* 2019; **127:** 1596–11.
4 Gelfand HM, Posch J. The recent outbreak of smallpox in Meschede, west Germany. *Am J Epidemiol* 1971; **93:** 234–37.
5 Morawska L, Milton DK. It is time to address airborne transmission of coronavirus disease 2019 (COVID-19). *Clinical Infect Dis* 2020; **71:** 2311–13.
6 Lewis D. Superspreading drives the COVID pandemic—and could help to tame it. *Nature* 2021; **590:** 544–46.

7 Eichler N, Thornley C, Swadi T, et al. Transmission of severe acute respiratory syndrome coronavirus 2 during border quarantine and air travel, New Zealand (Aotearoa). *Emerging Infect Dis* 2021; published online March 18. https://doi.org/10.3201/eid2705.210514.

8 Johansson MA, Quandelacy TM, Kada S, et al. SARS-CoV-2 transmission from people without COVID-19 symptoms. *JAMA Netw Open* 2021; **4:** e2035057.

9 Chen W, Zhang N, Wei J, Yen H-L, Li Y. Short-range airborne route dominates exposure of respiratory infection during close contact. *Building Environ* 2020; **176:** 106859.

10 Bulfone TC, Malekinejad M, Rutherford GW, Razani N. Outdoor transmission of SARS-CoV-2 and other respiratory viruses: a systematic review. *J Infect Dis* 2021; **223:** 550–61.

11 Klompas M, Baker MA, Rhee C, et al. A SARS-CoV-2 cluster in an acute care hospital. *Ann Intern Med* 2021; published online Feb 9. https://doi.org/10.7326/M20-567.

12 Van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *New Engl J Med* 2020; **382:** 1564–67.

13 Lednicky JA, Lauzard M, Fan ZH, et al. Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients. *Int J Infect Dis* 2020; **100:** 476–82.

14 Lednicky JA, Lauzardo M, Alam MM, et al. Isolation of SARS-CoV-2 from the air in a car driven by a COVID patient with mild illness. *medRxiv* 2021; published online Jan 15. https://doi.org/10.1101/2021.01.12.21249603 (preprint).

15 Fennelly KP. Particle sizes of infectious aerosols: implications for infection control. *Lancet Respir Med* 2020; **8:** 914–24.

16 Nissen K, Krambrich J, Akaberi D, et al. Long-distance airborne dispersal of SARS-CoV-2 in COVID-19 wards. *Sci Rep* 2020; **10:** 1–9.

17 Kutter JS, de Meulder D, Bestebroer TM, et al. SARS-CoV and SARS-CoV-2 are transmitted through the air between ferrets over more than one meter distance. *Nat Commun* 2021; **12:** 1–8.

18 Schijven J, Vermeulen LC, Swart A, Meijer A, Duizer E, de Roda Husman AM. Quantitative microbial risk assessment for airborne transmission of SARS-CoV-2 via breathing, speaking, singing, coughing, and sneezing. *Environ Health Perspect* 2021; **129:** 47002.

19 Sun K, Wang W, Gao L, et al. Transmission heterogeneities, kinetics, and controllability of SARS-CoV-2. *Science* 2021; **371:** eabe2424.

20 Laxminarayan R, Wahl B, Dudala SR, et al. Epidemiology and transmission dynamics of COVID-19 in two Indian states. *Science* 2020; **370:** 691–97.

21 Petersen E, Koopmans M, Go U, et al. Comparing SARS-CoV-2 with SARS-CoV and influenza pandemics. *Lancet Infect Dis* 2020; **20:** e238–44.

22 Guerra FM, Bolotin S, Lim G, et al. The basic reproduction number (R_0) of measles: a systematic review. *Lancet Infect Dis* 2017; **17:** e420–28.

23 Endo A, Abbott S, Kucharski AJ, Funk S. Estimating the overdispersion in COVID-19 transmission using outbreak sizes outside China. *Wellcome Open Res* 2020; **5:** 67.

24 Goldman E. Exaggerated risk of transmission of COVID-19 by fomites. *Lancet Infect Dis* 2020; **20:** 892–93.

25 Tang JW, Bahnfleth WP, Bluyssen PM, et al. Dismantling myths on the airborne transmission of severe acute respiratory syndrome coronavirus (SARS-CoV-2). *J Hosp Infect* 2021; **110:** 89–96.