Title
A paradigm shift to combat indoor respiratory infection

Journal
Science, 372(6543)

ISSN
0036-8075

Authors
Morawska, Lidia
Allen, Joseph
Bahnfleth, William
et al.

Publication Date
2021-05-14

DOI
10.1126/science.abg2025

Peer reviewed

Prevention of community respiratory infection transmission: a new era must start now

Lidia Morawska[1,2,*], Joseph Allen[3], William Bahnfleth[4], Philomena M. Bluyssen[5], Atze Boerstra[6], Giorgio Buonanno[7], Junji Cao[8], Stephanie J. Dancer[9], Andres Floto[10], Francesco Franchimon[11], Trisha Greenhalgh[12], Charles Haworth[13], Jaap Hogeling[14], Christina Isaxon[15], Jose L. Jimenez[16], Jarek Kurnitski[17], Yuguo Li[18], Marcel Loomans[19], Guy Marks[20], Linsey C. Marr[21], Livio Mazzarella[22], Arsen Krikor Melikov[23], Shelly Miller[24], Donald K. Milton[25], William Nazaroff[26], Peter V. Nielsen[27], Catherine Noakes[28], Jordan Peccia[29], Kim Prather[30], Xavier Querol[31], Chandra Sekhar[32], Olli Seppänen[33], Shin-ichi Tanabe[34], Julian W. Tang[35], Raymond Tellier[36], Kwok Wai Tham[37], Pawel Wargocki[23], Aneta Wierzbicka[15], Maosheng Yao[38]

[1,*] International Laboratory for Air Quality and Heath, Queensland University of Technology, Brisbane, Australia. Email: l.morawska@qut.edu.au
[2] Global Centre for Clean Air Research (GCARE), Department of Civil and Environmental Engineering, Faculty of Engineering and Physical Sciences, University of Surrey, Guildford GU2 7XH, United Kingdom
[3] Department of Environmental Health, Harvard T.H. Chan School of Public Health, USA
[4] Department of Architectural Engineering, The Pennsylvania State University, USA
[5] Faculty of Architecture and the Built Environment, Delft University of Technology, The Netherlands
[6] REHVA (Federation of European Heating, Ventilation and Air Conditioning Associations), BBA Binnenmilieu, The Netherlands
[7] Department of Civil and Mechanical Engineering, University of Cassino and Southern Lazio, Cassino, Italy
[8] Institute of Atmospheric Physics. Chinese Academy of Sciences, Xi'an, China, Beijing, China
[9] Edinburgh Napier University and NHS Lanarkshire, Scotland
[10] Department of Medicine, University of Cambridge, United Kingdom
[11] Franchimon ICM, The Netherlands
[12] Department of Primary Care Health Sciences, University of Oxford, Oxford, UK
[13] Cambridge Centre for Lung Infection, Royal Papworth Hospital and Department of Medicine, University of Cambridge, United Kingdom
[14] International Standards at ISSO, ISSO International Project, The Netherlands
[15] Ergonomics and Aerosol Technology Lund University, Lund, Sweden
[16] Department of Chemistry, and Cooperative Institute for Research in Environmental Sciences (CIRES), University of Colorado, Boulder, USA
[17] REHVA Technology and Research Committee, Tallinn University of Technology, Estonia
[18] Department of Mechanical Engineering, Hong Kong University, University of Hong Kong, Pokfulam, Hong Kong, China.
[19] Department of the Built Environment, Eindhoven University of Technology (TU/e), The Netherlands
[20] Centre for Air quality Research and evaluation (CAR), University of New South Wales (UNSW), Sydney, New South Wales, Australia
[21] Civil and Environmental Engineering, Virginia Tech, USA
[22] AiCARR, Politecnico di Milano, Italy
[23] International Centre for Indoor Environment and Energy, Department of Civil Engineering, Technical University of Denmark, Denmark
[24] Mechanical Engineering, University of Colorado, Boulder, USA
[25] Environmental Health, School of Public Health, University of Maryland, USA
[26] Department of Civil and Environmental Engineering, University of California, Berkeley, California, USA
[27] Faculty of Engineering and Science, Department of Civil Engineering, Aalborg University, Denmark
[28] School of Civil Engineering, University of Leeds, United Kingdom
[29] Environmental Engineering, Yale University, USA
[30] NSF Center for Aerosol Impacts on Chemistry of the Environment (CAICE), UC San Diego, USA
[31] Institute of Environmental Assessment and Water Research, Department of Geosciences, Spanish National Research Council, Barcelona, Spain
[32] Department of Building, National University of Singapore, Singapore
[33] Aalto University, Finland
[34] Department of Architecture, Waseda University, Japan
[35] Respiratory Sciences, University of Leicester, Leicester, United Kingdom
[36] Department of Medicine McGill University, Canada
[37] Department of Building, National University of Singapore, Singapore
[38] College of Environmental Sciences and Engineering, Peking University, Beijing, China

Abstract

Children and adults around the world suffer multiple airborne respiratory infections each year. Infections cause suffering, deaths, massive economic loss and disrupt the functioning of the society. Despite this, for numerous reasons, respiratory infections are considered an inescapable part of daily life. Very little has been done to limit their impact, and their prevention still awaits a systematic approach. However, we argue that it does not have to be this way. We need a profound change in how we view this risk and how we apply scientific knowledge, building engineering solutions and public health policies to reduce it. This change will lead to clean air with a significantly reduced pathogen count, which will improve people's health, together with societal economic benefits. While the scale of the changes required is enormous, this is not beyond the capabilities of our society, as has been shown in relation to food and waterborne disease, which have largely been controlled and monitored.

Disparity in approaches to different sources of environmental infections

There is great disparity in the way we think about different sources of environmental infection. For drinking water or food, most developed countries would not tolerate a risk of infection greater than 1 in 10,000. Yet in these same countries, children have multiple respiratory infections every year, with influenza a major cause of death in the elderly (*1-8*). Governments for the last 150 years have promulgated a large amount of legislation and invested heavily in sanitation and drinking water for public health purposes. However, respiratory infections continue to be regarded as an unavoidable part of daily life, with the measures governments suggest being like “shifting deckchairs on the Titanic” (*9*). Which means, up until now, governments did not really take notice of the iceberg below water level, e.g., the consequences of airborne respiratory infectious diseases and a pandemic of the scale of COVID-19. Being ‘surprised’ by the pandemic, short-term actions cannot provide a solution to deal with the iceberg below the water. It is argued that it would take large investments in infrastructure and changes in social behavior to reduce respiratory infections, whereas in fact the impact would likely be less than one percent increase in the construction cost of a typical building (*10*, *11*). For a building as a whole, Evans et al. (1998) (*12*) show a ratio of costs of 1:5:200, where for every dollar spent on construction cost, five are spent on maintenance and building operating costs and $200.00 on staffing and business operating costs. For the vast inventory of existing buildings, although the economic estimations are more complex due to a large number of variables, there are also numerous cost-effective solutions enhancing their performance to minimize the risk of infection transmission. Two factors may have contributed to our relatively weak approach to fighting airborne transmission of infectious diseases when compared with our strategies to prevent waterborne and foodborne transmission.

First, it is much harder to trace airborne infections than those that are waterborne or foodborne. Food and water contamination nearly always come from an easily identified point source with a discrete reservoir, such as a pipe, well, or package of food. Its impact on human health is also early if not immediate in terms of characteristic signs and symptoms, so that diligent epidemiology can track and identify the source relatively easily. Over the years, this has led to the establishment of current public health structures in well-resourced countries. We have standards enacted for all aspects of food and water processing, as well as wastewater and sewage. Public health officials, environmental health officers, and local councils are trained in surveillance, sampling, and investigation of any clusters of potential food and waterborne outbreaks, often alerted by local microbiology laboratories. There are published infection rates for a large range of pathogens, with morbidity and mortality risks now well established. For example, in Scotland, there have been high profile outbreaks of *Escherichia coli* 0157, *Salmonella* and *Listeria* spp. over the last few years, and annual spring-time alerts for cryptosporidium, the latter necessitating a ban on water consumption and council supply of bottled water (*13-16*). The latest outbreaks were community cases of *Clostridioides difficile*, which have been linked to main water supplies (*17*). By contrast, airborne studies are much more difficult to conduct because air as a contagion medium is nebulous, widespread, not owned by anybody, and uncontained. Airborne studies are also difficult because buildings and their airflows are complicated, and the measurements methods for such studies are also complex and not generally standardized.

Second, a long-standing misunderstanding and lack of research into airborne transmission of pathogens has negatively impacted an otherwise wider recognition of the significance of this route (*18*). In our modern era, most building construction has occurred subsequent to a decline in the belief that airborne pathogens are important, driven by a range of factors including the influential work of Charles V Chapin 1910, who denied an important role of airborne transmission of contagious diseases (*19*). Therefore, the design and construction of modern buildings make no modifications for this airborne risk, and as such, respiratory outbreaks have been repeatedly ‘explained away’ by the arguments of droplet transmission and handwashing. On one hand, John Snow’s (*20*) work correctly highlighted waterborne infections like cholera as a major public health risk, while on the other hand, Chapin downplayed the airborne public health risk – and building regulations for water vs air sanitation may have diverged in their emphasis because of this. For decades, the focus of architects and building engineers was on thermal comfort, odor control, initial investment cost, energy use and other performance issues, and as Janssen (*21*) suggested, the neglect of infection control could in part be based on perceived risk or on the assumption that there are more important ways to control infectious disease, despite ample evidence that healthy indoor environments with a significantly reduced pathogen count are essential for public health. Therefore, it is not surprising that there are investigative and preventive structures, and legislation for food and water-borne incidents, but almost nothing for airborne contagion.

We envision airborne infection policies similar to those for food and water be instituted within public health over the next decade. For this to happen, however, there is a need for a paradigm shift in how we view the transmission of respiratory infections to protect present and future generations from unnecessary suffering and economic losses due to the direct and indirect cost of the infections. This means a fundamental change in how we apply the science of infection transmission to every aspect of modern society to reduce this risk. It starts with a recognition that preventing respiratory infection, like reducing waterborne or foodborne disease, is a tractable problem.

Science and engineering of respiratory infection transmission

Over the past decades, we have witnessed a dramatic growth in our understanding of the mechanisms behind respiratory infection transmission, across all the relevant scientific disciplines, including microbiology, immunology, aerosol physics and building sciences. We know that respiratory infections are caused by pathogens emitted through the nose or mouth of an infected person and transported to a susceptible host. The pathogens are encapsulated in fluid-based particles aerosolised from sites in the respiratory tract during respiratory activities such as breathing, speaking/singing/shouting, sneezing, and coughing. The particles encompass a wide size range, but most lie within the range from sub-micrometres to a few micrometres (*22*, *23*).

We also understand that in immediate proximity to the source – the face of an infected person – the concentration of particles of all sizes is the highest. This is where the infection risk of a susceptible individual is the largest, either by inhalation of particles in exhaled plumes (*24*), or by deposition of the particles on the mucous membranes and further inoculation through the mouth, nose, or eyes (*25*). While individuals can be infected in close proximity, community outbreaks of infection most frequently occur at larger distances through the inhalation of airborne virus-laden particles in indoor spaces shared with infected individuals (*26*, *27*). Airborne transmission is potentially the dominant mode of transmission of numerous respiratory infections, including influenza (*28*), rhinoviruses (*29*, *30*), tuberculosis (*31*, *32*), measles (*33*), Middle East respiratory syndrome coronavirus (MERS-CoV) (*34*), respiratory syncytial virus (RSV) (*35*) and, as recently shown, COVID-19 (*25*, *36*, *37*), in shared room air as close range aerosol transmission (*25*) and superspreading events (*38*). By contrast, fomites play a much smaller role in overall infection transmission (*38*, *39*).

We also have strong evidence that the way we design, operate, and maintain our buildings influences transmission. Evidence about this emerges from the COVID-19 outbreaks already investigated, for example during choir practice (*40*, *41*), in a restaurant (*42*), on a cruise liner (*43*). There is also evidence from past studies on other diseases, for example, from the SARS-CoV-1 epidemic (*44*), or in relation to other diseases, for example, measles at schools (*45*-*51*). In each of these cases, inadequate ventilation contributing to high levels of infectious aerosol proved to be a critical problem.

Yet, before COVID-19, to the best of our knowledge, almost no engineering based measures to limit community respiratory infection transmission had been employed in public buildings (excluding health care facilities) or transport infrastructure anywhere in the world, despite the frequency of such infections, and despite the very large health burden and economic losses they cause (*52*). The key engineering measure is ventilation, supported by air filtration and air disinfection (*53*). In this context, ventilation includes a minimum amount of outdoor air combined with recirculated air that is cleaned using effective filtration and disinfection. There are of course ventilation guidelines and standards to which architects and building engineers must adhere: are they inadequate to mitigate indoor respiratory infection transmission?

Future ventilation systems to control respiratory infection transmission

The objectives of the existing guidelines and regulations regarding building ventilation are to address the issues of odor and occupant-generated carbon dioxide (CO_2), which is indicative of bioeffluent production, by specifying minimum ventilation rates and other measures to provide an acceptable IAQ for most occupants. Similarly, there are other guidelines and regulations to ensure thermal comfort. To achieve this, the amount of outdoor air delivered to indoor spaces is recommended or mandated in terms of set values of air change rate per hour, or liters of air per person per second (L/person/s). There are also prescribed threshold values of CO_2 and a range of indoor air temperatures and relative humidity. Different to the above are health-based indoor air quality guidelines. The most important is the World Health Organization (WHO) Indoor Air Quality (IAQ) guidelines, providing guideline values for benzene, carbon monoxide, formaldehyde, naphthalene, nitrogen dioxide, polycyclic aromatic hydrocarbons, radon, trichloroethylene and tetrachloroethylene, based on the duration of exposure (*54*). There are, however, no ventilation guidelines or standards set to specifically control the concentration of these pollutants indoors. The WHO *Dampness and Mold* guidelines do not recommend specific concentration limit values of mold, and reasons for this are explained in the document (*55*). None of the above or any other documents provide recommendations or standards for mitigating bacteria or viruses in indoor air, originating from human respiratory activities. Therefore, we need to reconsider the objective of ventilation to include not only the control of CO_2 and odor levels to ensure acceptable IAQ for a vast majority of occupants but also air pollutants linked to health effects AND airborne pathogens. Can this be achieved based on existing knowledge, by setting new required ventilation rate values? The challenge is that the ventilation rates required to protect against infection transmission cannot be derived in the same way as the rates for other pollutants.

Firstly, the ventilation rates must be risk-based rather than absolute, which means they need to be developed based on the assessment of the infection risk, considering the pathogen emission rates and the infectious dose with respect to which exists a body of data for a number of diseases, including influenza, SARS-CoV-1, MERS, TB, SARS-CoV-2 (*56*-*61*). Part of the challenge is also that we often have limited knowledge of viral emission rates, and they differ depending on the physiology of the respiratory tract (which varies with age, for example), the stage of the disease, and the type of respiratory activity (e.g., loud speaking, singing, or heavy breathing during sport or exercise). It is worthwhile to note, regarding the infectious dose, that it may differ depending on the mode of transmission. This is well established for influenza A where the infectious dose is smaller with an aerosol inoculum than with nasal instillation (*28*). Furthermore, some infectious agents display “anisotropy”, where the severity of disease vary according to the mode of transmission (*62*), e.g., for influenza and smallpox aerosol inocula are associated with more severe illness (*28*, *62*).

Secondly, future ventilation systems with higher airflow rates and distributing the supplied clean/disinfected air so that it reaches the breathing zone of occupants must be demand controlled and thus be flexible: the ventilation rate will differ for different venues according to the activities conducted there (e.g., higher ventilation rates will be required for gyms because of higher emissions during exercising, than for movie theatres – quiet resting), while considering all other parameters. While this may sound complicated due to the inherent need to consider room and micro-environment air distribution aspects, there are already models enabling assessments of ventilation rates and their effective distribution in the occupant microenvironments (*40*), and in general this is a rapidly expanding field. Demand control and flexibility are necessary not only to control the risk, but also to address other requirements including the control of indoor air pollution originating from inside and outside sources and, very importantly, to control energy use: higher ventilation means higher energy use; therefore, ventilation should be made adequate on demand, but not unreasonably high while considering energy, sick building syndrome symptoms and thermal comfort. Energy consumption associated with control of the indoor environment is a critical concern, given that buildings consume over 36% of energy globally (*63*), and the associated emissions contributing to climate affecting pollutants. Much of this energy is expended on heating/cooling outdoor air as it is brought indoors to maintain indoor air quality and, in some cases, thermal comfort. Therefore, while building designs should optimize the indoor environment quality in terms of health and comfort, they should do that in an energy-efficient way in the context of local climate and outdoor air pollution.

Thirdly, in some settings it will not be possible to increase ventilation to the point of reducing the risk to an acceptable level, regardless of the quality of the ventilation system. This refers to either the individual risk of infection for each susceptible occupant or to the event reproduction number, the expected number of new infections arising from a single infectious occupant at an event (*64*). Management of the event reproduction number is very important for the control of an epidemic, especially for indoor spaces with a high density of people, high emission rate (vocalization or exercising), and long periods of shared time. Spaces like this will require air purification measures, including air filtration and disinfection, enabling additional risk reduction. Air filtration can be achieved by incorporating filters into the building heating, ventilation and air conditioning (HVAC) system or by portable air purifiers (*65*), and air disinfection can be achieved by using ultraviolet (UV) devices (*53*). Importantly, the necessity of such measures and their effective per-person additional removal rate, and thus their efficacy in risk reduction, can be incorporated into the risk assessment and prospectively modelled.

The growing evidence of airborne transmission of respiratory infections through shared room air requires a shift in the way we think about ventilation and air purification measures (as discussed above), in order for them to become intrinsic to the way we operate as a modern urbanized society residing indoors over 90% of the time. It does not mean that every indoor space should became a biosafety facility, but it means that a building should be designed and operated according to its purpose and according to the activities conducted there, so that the airborne infection risk is lowered to below an acceptable level (Figure 1). A critical problem is that such measures cannot easily be taken during the pandemic because most current building systems have not been designed for limiting respiratory infection, building operators owners and operators were not trained to operate the systems during the pandemic, and ad hoc measures are often not sufficient. Appropriate and regular training for building operators and owners with emphasis on appropriate measures that can be implemented should form a part of national strategies in prevention of spread of airborne diseases/infections.

The only type of facilities where airborne infection control exists are health care facilities; in hospitals, clinical risk evaluation is a norm, because rarely is there full evidence available to support many of the measures taken for preventing infection. The requirements for hospital ventilation rates are typically significantly higher than for other public buildings. For example, the clean airflow rates recommended for infection control are more than double those specified for other buildings for control of odors and chemical air contaminants, according to the American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE) Standard 170 for healthcare and Standard 62.1 for other non-residential buildings (*66*, *67*). However, while modern hospitals comply with the relevant standards set to control infection, this may not always be the case for some hospitals that are still located in very old buildings as are still found in the UK, other European countries, and Quebec, Canada; such hospitals run into the interesting problem that some are in fact old enough (prior to the late 19th century) to have been designed according to the old anti-miasma theory that outside air has to be prevented from getting in. In modern times, overzealous interpretation of energy efficiency standards may lead to the same issue.

Clearly, comparing health care ventilation requirements with those for non-healthcare venues suggests that non-healthcare rates should be higher for effective infection control or that more recirculation with better filtration should be used.

The paradigm shift we need is, however, much deeper than simply rethinking how we design and operate buildings and transport; it must start at a much higher level than it did a century ago, as facilitated by public health physicians. It requires a change in how humanity thinks about respiratory infection transmission. This means in the first instance introducing, changing and extending the way hygiene is taught in schools, how medical students are trained, and how students of every relevant discipline related to this topic, from public health to engineering, should be taught. Secondly, there needs to be a shift in the perception that we cannot afford the cost of control, since the economic costs of infections by far exceed the initial infrastructure costs to contain them. For example, in the USA alone the yearly cost (direct and indirect) of influenza has been calculated at 11.2 billion in 2018 (*68*); for respiratory infections other than influenza, the yearly cost stood at 40 billion in 2003 (*69*). As well, when the final tally of the economic cost of the current pandemic will be available it will provide an even more striking example of the cost incurred through inaction. These costs are paid from different pockets than operating or health care costs, and there is often resistance to higher initial expenditure; ultimately, however, society pays all the costs. In any complex system, costs and benefits are never evenly distributed. It is inevitably the case that investment in one part of the system generates savings in a different part of the system, so cross-system reallocation of budgets must be facilitated or we get impasse. The benefits extend beyond infectious disease transmission. An improvement in indoor air quality will reduce absenteeism in the workplace from other, non-infectious causes, such as sick-building syndrome and allergic reactions, to the extent that the reduction in productivity losses will cover the cost of any ventilation changes required (*70*).

Proactive measures to reduce airborne transmission of respiratory diseases would align very closely with the Sustainable Development Goals (SDGs) proposed in 2015 by the United Nations to secure health and wellbeing for all humans (*71*). The SDGs were adopted by all 193 UN Member States in 2015, who committed to mobilize human and financial resources towards an ambitious *"plan of action for people, planet and prosperity"*. SDG3 is dedicated to health, while several other SDGs address environmental, political, social and economic determinants of health and well-being. The SDGs were presented as a paradigm shift from a relatively selective focus on specific diseases in the Millennium Development Goals (MDGs) towards a holistic vision of health and well-being which includes a healthy environment.

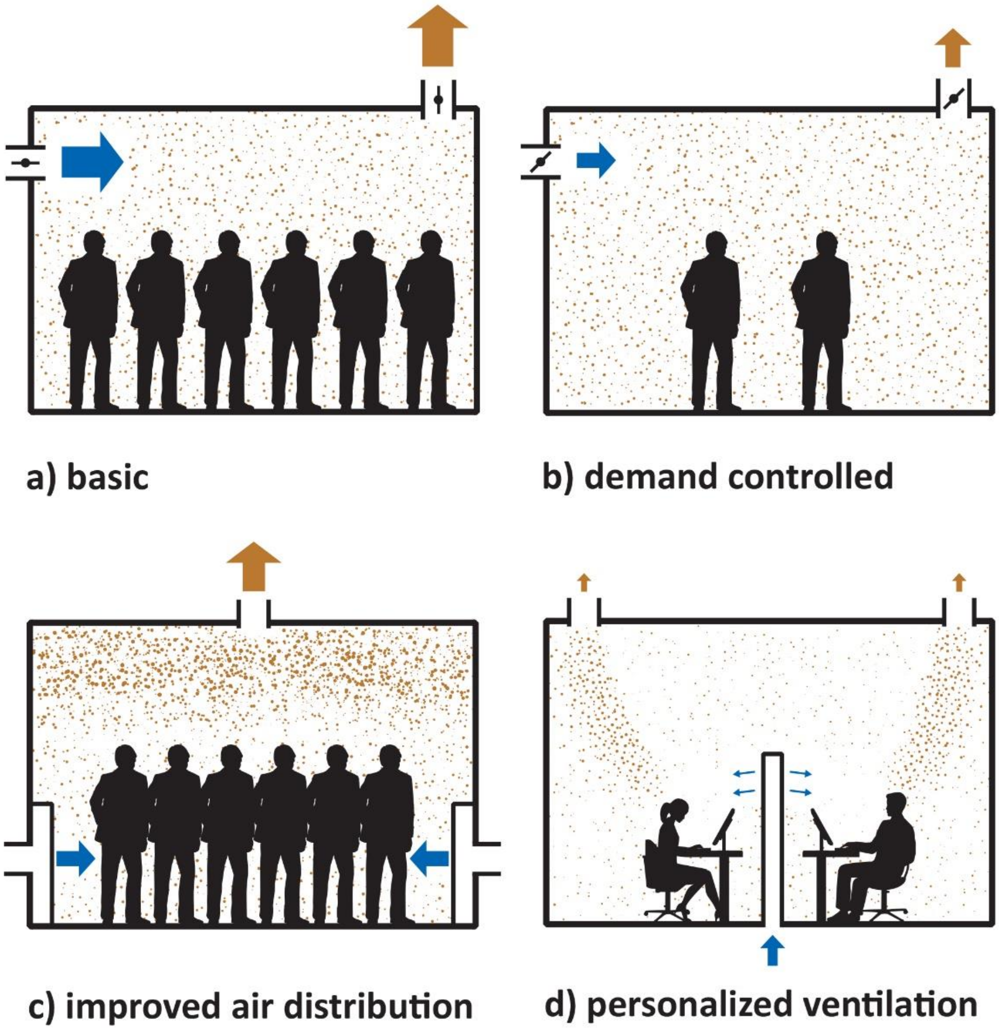

Figure 1. There must be a fundamental change in how we apply science of infection transmission to limit community respiratory infection transmissions in all our environments, dependent on their purpose and activities. Ventilation airflow rates must be controlled by the number of occupants in the space and their activity a) and b); better air distribution c) decreases exposure and saves energy. With personalized ventilation d) exposure can be reduced further, and energy efficiency improved with personalized ventilation.

Pathway towards the Paradigm Shift

This profound paradigm shift cannot occur overnight, but it must start now, while the world is still enduring the pandemic, and before the painful lessons learnt from this pandemic are forgotten, just as the lessons from previous pandemics have been mostly forgotten. How are we to start this process? Here is the pathway we should follow:

The hazard of airborne respiratory infection must be recognized so the risk can be controlled. The continuous global hazard of airborne respiratory infection transmission, not only during a pandemic, but all through the year and in all public indoor spaces, has not been universally accepted, despite strong evidence to support it and no convincing evidence to refute it.

Global WHO IAQ guidelines must be extended to include airborne pathogens. The guidelines must recognize the need to control the hazard of airborne transmission of respiratory infections. This includes recommendations on preventive measures addressing all modes of respiratory infection transmission in a proper and balanced way, based on state-of-the-art science. The recently published WHO Ventilation Roadmap (*72*) is an important step in the right direction, however, it falls substantially short of a paradigm shift in terms of recognition of the hazard of airborne respiratory infection transmission, and in turn, the necessity of risk control.

National comprehensive IAQ standards must be developed, promulgated, and enforced by all countries. Some countries around the globe have IAQ standards, but none of them are comprehensive enough to include airborne pathogens. In most countries that have IAQ standards, there are no enforcement procedures in place. Most countries do not have any IAQ standards.

Comprehensive ventilation standards must be developed by professional engineering bodies. Organizations such ASHRAE and the Federation of European Heating, Ventilation and Air Conditioning Associations (REHVA) have ventilation standards, and during the COVID-19 pandemic they have proposed building and system related control actions and design improvements to mitigate the risk of infection (*73*, *74*). However, the standards must be improved to explicitly consider infection control in their statements of purposes and definitions. Further, new approaches must be developed to encourage implementation of the standards (e.g. ‘ventilation certificates’ similar to those that exist for food hygiene certification for restaurants).

Wide use of monitors displaying the state of IAQ must be mandated. At present, the general public is not aware of the significance of IAQ and have no means of knowing the condition of the indoor spaces they occupy and share with others. Sensor technologies exist to display numerous parameters characterizing IAQ, the most common of which is CO_2, but not exclusively. All the existing IAQ sensing technologies have limitations and there is no doubt that more research is needed to develop alternative indicator systems. However, visible displays will help keep building operators accountable for ensuring good IAQ, and will advance the public's awareness of the state of the indoor environment, leading to increased demand for a safe indoor environment.

The COVID-19 pandemic has revealed how unprepared the world was to respond to it, despite the knowledge gained from pandemics that have occurred over past centuries. As William Wells, a pioneer of aerosol transmission, lamented in 1945 (*75*), the effort to remove pathogens from drinking water and food had not been replicated for the air. Seven decades later, we find ourselves in a similar place. Our societies, both the general population and decision-makers, are acting in much the same way as societies did in the Middle Ages, when there was limited understanding of the causes of respiratory infections and when emerging science was often suppressed for a variety of reasons, some of which are still relevant today. Ironically, in the 19th century, significantly higher ventilation rates in buildings were recommended by physicians focused on infectious disease than nowadays. In the 20th century, engineers have led a major shift to design and operate systems to achieve a proper balance among thermal comfort, air quality and energy consumption (*21*), rather than for controlling respiratory infection transmission (*21*). The paradigm shift now has to be on the scale that occurred in 19th century Britain, when the publication of the *Sanitary Report* (*76*) led the government to encourage cities to organise clean water supplies and centralised sewage systems. In the 21st century we need to establish the foundations to ensure that the air in our buildings is clean with a significantly reduced pathogen count, contributing to the building occupants' health, just as we expect for the water coming out of our taps.

References

1. F. M. de Benedictis, A. Bush, Recurrent lower respiratory tract infections in children. *BMJ* **362**, k2698 (2018).
2. A. R. R. Freitas, M. R. Donalisio, Excess of mortality in adults and elderly and circulation of subtypes of influenza virus in Southern Brazil. *Frontiers in Immunology* **8**, 1903 (2018).
3. A. C. Hayward *et al.*, Effectiveness of an influenza vaccine programme for care home staff to prevent death, morbidity, and health service use among residents: cluster randomised controlled trial. *BMJ* **333**, 1241 (2006).
4. R. E. Jordan, J. I. Hawker, Influenza in elderly people in care homes. *BMJ* **333**, 1229 (2006).
5. A. Martínez *et al.*, Risk factors associated with severe outcomes in adult hospitalized patients according to influenza type and subtype. *PLoS One* **14**, e0210353 (2019).
6. P. K. Pattemore, L. C. Jennings, Epidemiology of respiratory infections. *Pediatric Respiratory Medicine*, 435-452 (2008).
7. S. E. Talbird *et al.*, Impact of population aging on the burden of vaccine-preventable diseases among older adults in the United States. *Human Vaccines & Immunotherapeutics*, 1-12 (2020).

8. S. Taylor *et al.*, Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. *Journal of Infection* **74**, 29-41 (2017).

9. P. H. E. NHS, "Infection control precautions to minimise transmission of acute respiratory tract infections in healthcare settings," (October 2016).

10. CDC. (Centers for Disease Control and Prevention, 2019).

11. REHVA *et al.*, "Indoor climate and productivity in offices," *REHVA Guidebook* (2006).

12. R. Evans, R. Haryott, N. Haste, A. Jones, *The long-term costs of owning and using buildings*. (The Royal Academy of Engineering, London, United Kingdom, 1998).

13. K. G. Pollock, D. Young, H. V. Smith, C. N. Ramsay, Cryptosporidiosis and filtration of water from Loch Lomond, Scotland. *Emerging Infectious Diseases* **14**, 115 (2008).

14. J. Cowden, S. Ahmed, M. Donaghy, A. Riley, Epidemiological investigation of the central Scotland outbreak of Escherichia coli O157 infection, November to December 1996. *Epidemiology & Infection* **126**, 335-341 (2001).

15. E. Okpo *et al.*, An outbreak of an unusual strain of Listeria monocytogenes infection in North-East Scotland. *Journal of Infection and Public Health* **8**, 612-618 (2015).

16. R. M. Thomson, H. J. Henderson, A. Smith-Palmer, An outbreak of Salmonella Saintpaul in a Scottish childcare facility: the influence of parental under-reporting. *BMC Infectious Diseases* **19**, 847 (2019).

17. S. M. Kotila *et al.*, Clostridium difficile contamination of public tap water distribution system during a waterborne outbreak in Finland. *Scandinavian Journal of Public Health* **41**, 541-545 (2013).

18. L. Morawska, D. K. Milton, It is time to address airborne transmission of COVID-19. *Clinical Infectectious Diseases* **6**, ciaa939 (2020).

19. C. V. Chapin, *The sources and modes of infection*. (John Wiley & Sons, New York, USA, 1910), vol. First Edition, First Thousand.

20. J. Snow, *On the mode of communication of cholera*. (London, United Kingdom, 1855).

21. J. E. Janssen, The history of ventilation and temperature control: The first century of air conditioning. *ASHRAE Journal* **41**, 48 (1999).

22. L. Morawska *et al.*, Size distribution and sites of origin of droplets expelled from the human respiratory tract during expiratory activities. *Journal of Aerosol Science* **40**, 256-269 (2009).

23. G. Zayas *et al.*, Effectiveness of cough etiquette manoeuvres in disrupting the chain of transmission of infectious respiratory diseases. *BMC Public Health* **13**, 811 (2013).

24. K. A. Prather *et al.*, Airborne transmission of SARS-CoV-2. *Science (New York, NY)*, eabf0521 (2020).

25. W. Chen, N. Zhang, J. Wei, H.-L. Yen, Y. Li, Short-range airborne route dominates exposure of respiratory infection during close contact. *Building and Environment*, 106859 (2020).

26. S. Riley *et al.*, Community prevalence of SARS-CoV-2 virus in England during May 2020: REACT study. *medRxiv*, (2020).

27. M. Kriegel *et al.*, Predicted Infection Risk for Aerosol Transmission of SARS-CoV-2. *medRxiv*, (2020).

28. R. Tellier, Review of aerosol transmission of influenza A virus. *Emerging Infectious Diseases* **12**, 1657 (2006).

29. N. H. Leung *et al.*, Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nature Medicine* **26**, 676-680 (2020).

30. T. A. Myatt *et al.*, Detection of airborne rhinovirus and its relation to outdoor air supply in office environments. *American Journal of Respiratory and Critical Care Medicine* **169**, 1187-1190 (2004).

31. A. R. Escombe *et al.*, The detection of airborne transmission of tuberculosis from HIV-infected patients, using an in vivo air sampling model. *Clinical Infectious Diseases* **44**, 1349-1357 (2007).

32. R. Riley *et al.*, Aerial dissemination of pulmonary tuberculosis. A two-year study of contagion in a tuberculosis ward. *American Journal of Epidemiology* **142**, 3-14 (1995).

33. A. B. Bloch *et al.*, Measles outbreak in a pediatric practice: airborne transmission in an office setting. *Pediatrics* **75**, 676-683 (1985).

34. S.-H. Kim *et al.*, Extensive Viable Middle East Respiratory Syndrome (MERS) Coronavirus Contamination in Air and Surrounding Environment in MERS Isolation Wards. *Clinical Infectious Diseases* **63**, 363-369 (2016).

35. H. Kulkarni *et al.*, Evidence of respiratory syncytial virus spread by aerosol. Time to revisit infection control strategies? *American Journal of Respiratory and Critical Care Medicine* **194**, 308-316 (2016).

36. J. A. Lednicky *et al.*, Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients. *International Journal of Infectious Diseases*, (2020).

37. S. Tang *et al.*, Aerosol transmission of SARS-CoV-2? evidence, prevention and control. *Environment International* **144**, 106039 (2020).

38. D. Lewis, COVID-19 rarely spreads through surfaces. So why are we still deep cleaning. *Nature* **590**, 26-28 (2021).

39. UK-SAGE. (2020), vol. 2020.

40. G. Buonanno, L. Morawska, L. Stabile, Quantitative assessment of the risk of airborne transmission of SARS-CoV-2 infection: prospective and retrospective applications. *Environment International* **145**, 106112 (2020).

41. S. L. Miller *et al.*, Transmission of SARS-CoV-2 by inhalation of respiratory aerosol in the Skagit Valley Chorale superspreading event. *Indoor Air*, (2020).

42. J. Lu *et al.*, COVID-19 outbreak associated with air conditioning in restaurant, Guangzhou, China, 2020. *Emerging Infectious Diseases* **26**, (2020).

43. P. Azimi, Z. Keshavarz, J. G. C. Laurent, B. R. Stephens, J. G. Allen, Mechanistic Transmission Modeling of COVID-19 on the Diamond Princess Cruise Ship Demonstrates the Importance of Aerosol Transmission. *Proceedings of the National Academy of Sciences* **118**, e2015482118 (2020).

44. S. Xiao, Y. Li, T.-w. Wong, D. S. Hui, Role of fomites in SARS transmission during the largest hospital outbreak in Hong Kong. *PloS one* **12**, (2017).

45. Y. J. Choe *et al.*, An outbreak of measles in a university in Korea, 2014. *Journal of Korean Medical Science* **32**, 1876-1878 (2017).

46. K. B. Gibney, A. Brahmi, M. O’Hara, R. Morey, L. Franklin, Challenges in managing a school-based measles outbreak in Melbourne, Australia, 2014. *Australian and New Zealand Journal of Public Health* **41**, 80-84 (2017).

47. R. Ma *et al.*, A measles outbreak in a middle school with high vaccination coverage and evidence of prior immunity among cases, Beijing, PR China. *Vaccine* **34**, 1853-1860 (2016).

48. W. N. Pickles. (SAGE Publications, 1935).

49. E. Riley, G. Murphy, R. Riley, Airborne spread of measles in a suburban elementary school. *American Journal of Epidemiology* **107**, 421-432 (1978).

50. O. Wichmann *et al.*, Large measles outbreak at a German public school, 2006. *The Pediatric Infectious Disease Journal* **26**, 782-786 (2007).

51. L. F. Yeung *et al.*, A limited measles outbreak in a highly vaccinated US boarding school. *Pediatrics* **116**, 1287-1291 (2005).

52. W. J. Fisk, A. H. Rosenfeld, Estimates of improved productivity and health from better indoor environments. *Indoor Air* **7**, 158-172 (1997).

53. L. Morawska *et al.*, How can airborne transmission of COVID-19 indoors be minimised? *Environment International* **142**, 105832 (2020).

54. WHO, "Guidelines for Indoor Air Quality, Selected Pollutants " (World Health Organization, Geneva, 2010).

55. WHO, "WHO Guidelines for Indoor Air Quality - Dampness and Mould " (2009).

56. U. Adhikari *et al.*, A case study evaluating the risk of infection from Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV) in a Hospital Setting Through Bioaerosols. *Risk Analysis* **39**, 2608-2624 (2019).

57. R. M. Jones *et al.*, Characterizing the risk of infection from Mycobacterium tuberculosis in commercial passenger aircraft using quantitative microbial risk assessment. *Risk Analysis: An International Journal* **29**, 355-365 (2009).
58. A. Mikszewski, L. Stabile, G. Buonanno, L. Morawska, The airborne contagiousness of respiratory viruses: a comparative analysis and implications for mitigation. *medRxiv*, (2021).
59. T. Watanabe, T. A. Bartrand, T. Omura, C. N. Haas, Dose-response assessment for influenza A virus based on data sets of infection with its live attenuated reassortants. *Risk Analysis: An International Journal* **32**, 555-565 (2012).
60. T. Watanabe, T. A. Bartrand, M. H. Weir, T. Omura, C. N. Haas, Development of a dose-response model for SARS coronavirus. *Risk Analysis: An International Journal* **30**, 1129-1138 (2010).
61. X. Zhang, Z. Ji, Y. Yue, H. Liu, J. Wang, Infection risk assessment of COVID-19 through aerosol transmission: a case study of South China Seafood Market. *Environmental Science & Technology*, (2020).
62. D. M. Milton, What was the primary mode of smallpox transmission? Implications for biodefense. *Frontiers in Cellular and Infection Microbiology* **2**, 150 (2012).
63. UNE-IEA, "Global Status Report 2017: Towards a zero-emission, efficient, and resilient buildings and construction sector," (UN Environment and International Energy Agency (UNE-IEA), 2017).
64. E. A. Nardell, Wells Revisited: Infectious Particles vs. Quanta of Mycobacterium tuberculosis Infection–Don't Get Them Confused. *Mycobacterial Diseases* **6**, 1000231 (2016).
65. P. M. Bluyssen, M. Ortiz, D. Zhang, The effect of a mobile HEPA filter system on 'infectious' aerosols, sound and air velocity in the SenseLab. *Building and Environment*, 107475 (2020).
66. ASHRAE, "Ventilation of Health Care Facilities; ANSI/ASHRAE/ASHE Standard 170-2017," (American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE) 2017).
67. ASHRAE, "Ventilation for Acceptable Indoor Air Quality. ANSI/ASHRAE Standard 62.1-2019 " (2019).
68. W. C. Putri, D. J. Muscatello, M. S. Stockwell, A. T. Newall, Economic burden of seasonal influenza in the United States. *Vaccine* **36**, 3960-3966 (2018).
69. A. M. Fendrick, A. S. Monto, B. Nightengale, M. Sarnes, The economic burden of non–influenza-related viral respiratory tract infection in the United States. *Archives of Internal Medicine* **163**, 487-494 (2003).
70. W. J. Fisk, "Health and Productivity Gains from Better Indoor Environments and their Relationship with Building Energy Efficiency," *Annual Revue of Energy and the Environment 2000* (Lawrence Berkley National Laboratory, Berkley, California., 2000).
71. G. UN, Transforming our world: The 2030 agenda for sustainable development. A/RES/70/1, 21 October. (2015).
72. WHO, "Roadmap to improve and ensure good indoor ventilation in the context of COVID-19. World Health Organisation," (2021).
73. ASHRAE, "ASHRAE Position Document on Infectious Aerosols," (2020).
74. REHVA, "REHVA COVID-19 guidance document, August 3, 2020," (Federation of European Heating, Ventilation and Air Conditioning Associations (REHVA), 2020).
75. W. F. Wells, Sanitary ventilation by radiant disinfection. *The Scientific Monthly* **60**, 325-334 (1945).
76. E. Chadwick, "Report on the Sanitary Condition of the Labouring Population of Great Britain," (1842).