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Assessing microbial decontamination of indoor air with particular focus on human pathogenic viruses

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Transmission of bacterial, fungal, and viral pathogens is of primary importance in public and occupational health and infection control. Although several standardized protocols have been proposed to target microbes on fomites through surface decontamination, use of microbicidal agents, and cleaning processes, only limited guidance is available on microbial decontamination of indoor air to reduce the risk of pathogen transmission between individuals. This article reviews the salient aspects of airborne transmission of infectious agents, exposure assessment, in vitro assessment of microbicidal agents, and processes for air decontamination for infection prevention and control. Laboratory-scale testing (eg, rotating chambers, wind tunnels) and promising field-scale methodologies to decontaminate indoor air are also presented. The potential of bacteriophages as potential surrogates for the study of airborne human pathogenic viruses is also discussed.

Although the microbial world is rich in diversity, only a small portion of microbes represent a risk to human and animal health. However, the socioeconomic impact of such harmful microbes is enormous and represents an important worldwide challenge in public and occupational health and in veterinary medicine.[1] Among the vehicles for microbial spread, indoor air is perhaps the least understood, likely because of a general lack of standardized protocols to study the survival and removal or inactivation of airborne microbes. This is a brief review of airborne transmission of infectious agents, along with an assessment of available technologies for the decontamination of indoor air, with particular reference to human pathogenic viruses.

According to Roy and Milton,[2] certain types of pathogens are obligated to spread by air only; pulmonary tuberculosis is a good example of this.[3] Others may do so preferentially (eg, measles, varicella), and still others may be opportunistic with regard to their airborne spread (eg, smallpox, influenza, noroviruses). There are still others that may be carried by air to multiply in their host. For example, methicillin-resistant *Staphylococcus aureus* (MRSA) nasal carriage has been linked to exposure to contaminated air.[4]

For some airborne infectious agents, the respiratory system may not be the ultimate target. For example, epidemiologic evidence[5,6] suggests that airborne particles of human norovirus, a major cause of acute gastroenteritis, may first be retained in the tonsillar region, with subsequent translocation to the gastrointestinal tract. Recently, molecular analysis of air found evidence of norovirus in several areas of health care facilities.[7] The pandemic potential of human influenza viruses is related to their ability to spread by air.[8,9] In light of this evidence, safe and effective decontamination of indoor air would be an important adjunct to infection prevention and control.[10]

For most viral infections of humans, epidemiologic profiles correspond to direct-contact transmission through coughing, sneezing, or speaking-related emissions of pathogen-containing droplets and subsequent contact with the mouth or nose of a susceptible host. Droplets emitted by an infected person vary in size between 0.3 and 2,000 μm.[11-14] Although the general size range of pathogen-laden droplet nuclei is 0.5-5.0 μm, it is hypothesized that the microbe itself has little influence in this regard. The size of such particles is driven mainly by their solute content.[15]

The water content of air will influence the rate at which droplets will evaporate to become droplet nuclei (Fig 1). Droplet nuclei are preferentially formed at low relative humidity (RH), whereas high RH may favor maintenance and settling of droplets.[14]

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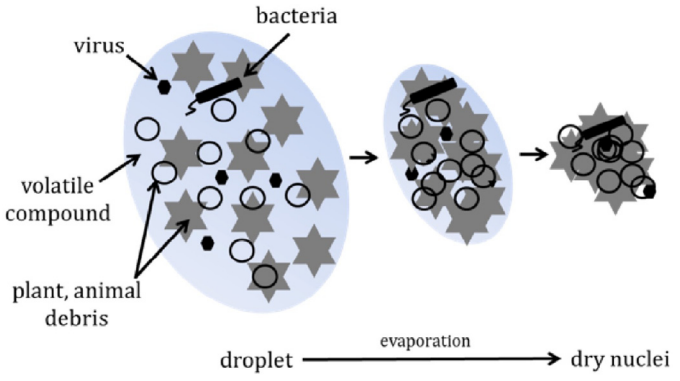

Fig 1. Droplet nuclei formation.

Influenza viruses were measured in the air of hospital emergency rooms in a National Institute for Occupational Safety and Health study. Over 50% of the detected viruses were found in the <5 μm fraction, suggesting their presence in airborne droplet nuclei.[16] Similar findings were obtained with other respiratory viruses: cytomegalovirus,[17] respiratory syncytial virus,[18] rhinovirus,[19] and the coronavirus responsible for the severe acute respiratory syndrome.[20]

EXPOSURE ASSESSMENT: FROM SAMPLING TO ANALYSIS

Indoor air often contains a varied and variable blend of microbes,[21] along with a cocktail of chemicals, allergens, and other particulates. Inhalation of such air may expose an individual to a combination of potentially harmful microbes and other factors simultaneously, making risk assessment a major challenge. For instance, individuals with preexisting respiratory allergies may react to an inhaled pathogen differently than individuals without respiratory allergies. Chronic smoking is also well known as a predisposing factor to respiratory pathogens.

In spite of the availability of a variety of methods for collecting microbes from indoor air,[22] efficient recovery and detection and quantitation of viable pathogens in field samples of air remain difficult. The generally low levels of airborne pathogens require the collection of hundreds of liters of air,[23] and such a process can be quite damaging to the viability of many types of pathogens, leading to an underestimation of their concentration. Often, the pathogen recovered may not grow in the laboratory. In addition, molecular approaches cannot readily distinguish between viable and nonviable microbes, therefore compromising their value in risk assessment and epidemiologic studies.

Among the major knowledge gaps in the aerobiology of human pathogens is the lack of understanding of size distribution of airborne particles carrying viable infectious agents.[24] Such knowledge (granulometry) will be crucial to the design, assessment, and deployment of indoor air decontamination technologies.

PHAGES AS MODELS FOR AIRBORNE VIRUSES

Phages are already used as models in several areas of research and field investigations. For example, in the pharmaceutic and food industries, the U.S. Food and Drug Administration recommends their use to test the effectiveness of filtration devices. They are also used as surrogates for enteric viruses in studies of wastewater treatment.[25] However, their potential as surrogates in the study of aerobiology of human pathogenic viruses remains underexplored, despite their common structural similarities with eukaryotic viruses. For example, phages can be enveloped or nonenveloped and can possess single- or double-stranded RNA or DNA genomes, which may be segmented, linear, or circular. The phage capsids also are of a variety of sizes and shapes reflective of human pathogenic viruses.[26] Our ability to culture and assay phages inexpensively and without the need for biosafety precautions also adds to their attraction as surrogates.

Recently, phage models have been developed and compared for appropriateness in simulating eukaryotic viruses in bioaerosols.[27] The resistance of various phages to environmental stresses (RH, ultraviolet [UV], temperature, and aerosol duration) was studied, and it was shown that the response to stresses varied between the various models.[28] Phage MS2 has been the most broadly used surrogate in aerosol studies and is used mostly in biodefense to predict the fate and transport of biothreat agents.[29] Table 1 presents the phage models used and validated.

Our laboratory has used phages to predict the most probable areas in a mechanically ventilated building where airborne viruses could be efficiently sampled and detected. Further, with a simple smoke test, it is possible to detect the less ventilated zones where pathogenic agents have higher odds of being concentrated.[30]

IN VITRO ASSESSMENT OF MICROBICIDAL AGENTS AND PROCESSES FOR INDOOR AIR DECONTAMINATION

Pathogenic agents may remain suspended in indoor air even in the absence of the infected person who is emitting them.[16] Hence, air decontamination should be implemented in situations such as room cleaning after the release of an infected patient or after a vomiting episode in a classroom. In the literature, most of the procedures developed to decontaminate air in occupied spaces were not validated in vitro with multiple model microorganisms or size-distributed microbial aerosols.

Although it would be highly desirable to assess any indoor air decontamination technology against all major types of airborne microbial threats before its adoption, time and cost constraints and the unavailability of suitable test protocols essentially preclude such an approach. Furthermore, the in-field efficiency of a given technology is also subject to numerous site-specific variables. This reinforces the need for well-designed experimental settings and robust test protocols and the selection of suitable surrogates for airborne pathogens to evaluate potential means of indoor air decontamination as thoroughly as possible. It should also be noted here that experimental aerosolization of infectious agents may increase the risk of biohazards in general, therefore requiring the need for proper staff training, the availability of proper personal protective equipment, and the institution of rigorous safety procedures.

Environmentally controlled aerosol-aging chambers are designed to simulate environmental stresses that are imposed on microbial aerosols in order to understand the role of environmental parameters, such as temperature, UV, and RH, on the fate of airborne infectious agents.[28] Aerosols can remain airborne for prolonged periods in rotating chambers[31] because these particles remain suspended in a rotating mass of air. The gravitational forces exerted on the particles are countered by centrifugal forces created by the rotation of the drum.[32] The effects on various viral and bacterial aerosols held at different levels of air temperature, RH, hydrogen peroxide vapor, UV radiation, ozone, and other physical and chemical agents can be studied using the rotating drum[28] (Caroline Duchaine, 2016). Figure 2 shows a picture of a rotating drum with the desiccants and the control panel.

AIR DECONTAMINATION FOR CONTROL OF INFECTIOUS AGENTS

Natural ventilation is the most important means of air decontamination, but it is not often applicable because of building design, climate, security, or pest control.[23] Mechanical ventilation is more