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Generic aspects of the airborne spread of human pathogens indoors and emerging air decontamination technologies

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Indoor air can be an important vehicle for a variety of human pathogens. This review provides examples of airborne transmission of infectious agents from experimental and field studies and discusses how airborne pathogens can contaminate other parts of the environment to give rise to secondary vehicles leading air-surface-air nexus with possible transmission to susceptible hosts. The following groups of human pathogens are covered because of their known or potential airborne spread: vegetative bacteria (staphylococci and legionellae), fungi (*Aspergillus*, *Penicillium*, and *Cladosporium* spp and *Stachybotrys chartarum*), enteric viruses (noro- and rotaviruses), respiratory viruses (influenza and coronaviruses), mycobacteria (tuberculous and nontuberculous), and bacterial spore formers (*Clostridium difficile* and *Bacillus anthracis*). An overview of methods for experimentally generating and recovering airborne human pathogens is included, along with a discussion of factors that influence microbial survival in indoor air. Available guidelines from the U.S. Environmental Protection Agency and other global regulatory bodies for the study of airborne pathogens are critically reviewed with particular reference to microbial surrogates that are recommended. Recent developments in experimental facilities to contaminate indoor air with microbial aerosols are presented, along with emerging technologies to decontaminate indoor air under field-relevant conditions. Furthermore, the role that air decontamination may play in reducing the contamination of environmental surfaces and its combined impact on interrupting the risk of pathogen spread in both domestic and institutional settings is discussed.

Air, a universal environmental equalizer, affects all living and non-living forms on planet earth. For humans, it has profound health implications in all indoor environments where we normally spend most of our time.[1-3] Air quality is also forever changing because of the influence of many controllable and uncontrollable factors that are virtually everywhere. Indoor air, in particular, can expose us to noxious chemicals, particulates, and a variety of infectious agents, as well as pollen and other allergens.[4,5]

Emerging pathogens, such as noroviruses[6] and *Clostridium difficile*,[7] have also been detected in indoor air, with a strong potential for airborne dissemination. Pathogens discharged into the air may settle on environmental surfaces, which could then become secondary vehicles for the spread of infectious agents indoors.[8] The possible transmission of drug-resistant bacteria by indoor air adds another cause for concern.[9] A combination of on-going societal changes is adding further to the potential of air as a vehicle for infectious agents.[10-12] The quality of indoor air is therefore a prominent public health concern[13,14] that requires a clear understanding of the transmission processes for the development and implementation of targeted infection prevention and control measures.[15]

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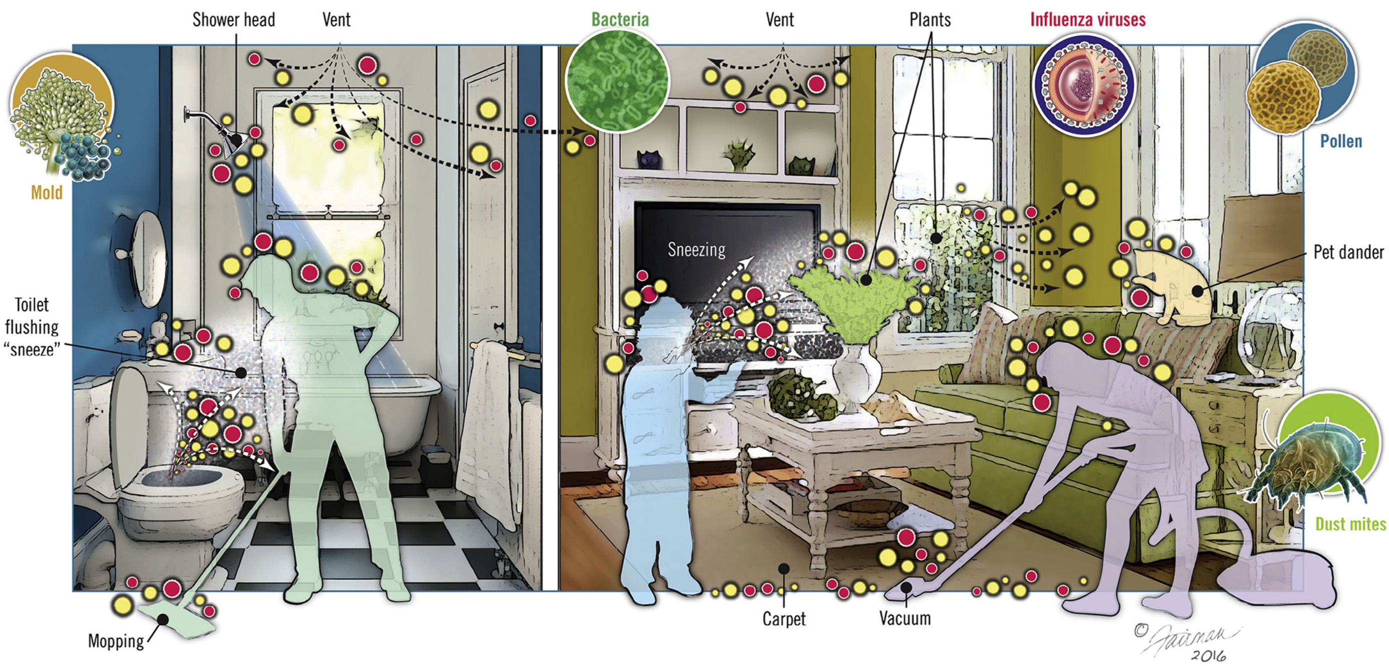

Fig 1. Sources of airborne pathogens indoors and potential for environmental surface contamination. These sources may include humans; pets; plants; plumbing systems, such as operational toilets and shower heads; heating, ventilation, vacuuming, mopping, and air-conditioning systems; resuspension of settled dust; and outdoor air. The yellow and red dots represent human pathogens or harmless microorganisms. Adapted with permission from BioMed Central.[23]

Although direct and indirect exposure to pathogens in the air can occur by other means, infections from the inhalation and retention, including translocation and ingestion after inhalation of droplet nuclei, are generally regarded as true airborne spread. Aerosols of various sizes that contain infectious agents can be emitted from a variety of sources, such as infected or colonized individuals[16] or flushing toilets, and may expose susceptible persons either directly (droplet transmission) or by remaining suspended in the air for inhalation (airborne transmission).[17,18] Contrary to the conventionally held belief, modeling work has redefined the Wells evaporation-falling curve,[19,20] revealing that expelled large droplets could be carried >6 m away by exhaled air at a velocity of 50 m/s (sneezing), >2 m away at a velocity of 10 m/s (coughing), and <1 m away at a velocity of 1 m/s (breathing), leading to potential transmission of short-range infectious agents that contain aerosols.[21]

Airborne transmission requires that pathogens survive the process of aerosolization and persist in the air long enough to be transmitted to a susceptible host.[22] Aerosolized pathogens may settle onto environmental surfaces in the immediate vicinity, leading to genesis of secondary vehicles (Fig 1).[23] This review provides current information on the spread of human pathogens by indoor air, with a focus on the major classes of human pathogens from experimental and field studies, and on emerging air decontamination technologies, including test protocols developed to assess their performance under field-relevant conditions.

METHODS FOR STUDYING AIRBORNE HUMAN PATHOGENS

The study of aerosolized human pathogens requires the ability to produce them experimentally at the appropriate size, store them, and sample them for residual infectious content over a predetermined time period.[13] The equipment must also simulate naturally occurring environmental conditions and the duration of exposure to accurately assess aerosol survivability.[24] Various analytical methods and air samplers have been used to characterize airborne pathogens and overcome the challenges of collecting and analyzing them. Relevant studies have been reviewed in detail elsewhere.[13,25,26]

ENVIRONMENTAL FACTORS THAT INFLUENCE AIRBORNE MICROBIAL SURVIVAL

Aerosolized microbes must survive the prevailing environmental conditions to potentially infect a susceptible host.[22] Multiple factors affect airborne survival of microbes indoors (Table 1).[13,31] The effect of these factors on different types of microbes varies, and generalizations can be difficult because of differences in the experimental methodologies used.[27] Air temperature, relative humidity (RH), and turbulence are among the more important factors affecting the fate and spread of infectious agents indoors.

The analysis of air samples for microbes now includes methods that are based on the polymerase chain reaction (PCR). However, PCR-based methods typically cannot differentiate between viable and nonviable microbes.[32] A recent study found that PCR substantially overestimated the quantity of infectious airborne influenza virus, but the differences in infectious versus noninfectious virus over time were similar to data from quantification by plaque-forming units, which determined that virus losses were evident within 30-60 minutes postaerosolization.[32] Generally, enveloped viruses survive better at lower RH, but there are many exceptions.[28] Other factors that affect aerosol activation in relation to RH include evaporative activity (ie, dehydration, rehydration), surface areas of particles, and pH.[28]

AIRBORNE SPREAD OF MAJOR CLASSES OF HUMAN PATHOGENS

Although studies with experimental animals have determined the susceptibility to airborne pathogens and the minimal infective inhalation dose of a given pathogen,[25] there are wide variations