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Commentary

Indoor air as a vehicle for human pathogens: Introduction, objectives, and expectation of outcome



Syed A. Sattar MSc, Dip Bact, MS, PhD *

Professor Emeritus of Microbiology, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada

Key Words:

Aerobiology
indoor air
airborne pathogens
air decontamination
airborne pollutants

Airborne spread of pathogens can be rapid, widespread, and difficult to prevent. In this international workshop, a panel of 6 experts will expound on the following: (1) the potential for indoor air to spread a wide range of human pathogens, plus engineering controls to reduce the risk for exposure to airborne infectious agents; (2) the behavior of aerosolized infectious agents indoors and the use of emerging air decontamination technologies; (3) a survey of quantitative methods to recover infectious agents and their surrogates from indoor air with regard to survival and inactivation of airborne pathogens; (4) mathematical models to predict the movement of pathogens indoors and the use of such information to optimize the benefits of air decontamination technologies; and (5) synergy between different infectious agents, such as legionellae and fungi, in the built environment predisposing to possible transmission-related health impacts of aerosolized biofilm-based opportunistic pathogens. After the presentations, the panel will address a set of preformulated questions on selection criteria for surrogate microbes to study the survival and inactivation of airborne human pathogens, desirable features of technologies for microbial decontamination of indoor air, knowledge gaps, and research needs. It is anticipated that the deliberations of the workshop will provide the attendees with an update on the significance of indoor air as a vehicle for transmitting human pathogens with a brief on what is currently being done to mitigate the risks from airborne infectious agents.

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“Clean air is a basic requirement of life. The quality of air inside homes, offices, schools, day care centres, public buildings, health care facilities or other private and public buildings where people spend a large part of their life is an essential determinant of healthy life and people’s well-being. . .” –World Health Organization, 2010

I welcome you all to this multinational workshop! This workshop was conceived over a year ago, and the organizing committee (Table 1) formally requested that ASTM International (www.astm.org/) hold the event under its auspices. ASTM’s Committee E35, which deals

with pesticides, antimicrobials, and alternative control agents, approved the proposal in April 2015.

Mounting recognition of indoor air as a vehicle for infectious agents is leading government regulators, such as the U.S. Environmental Protection Agency, to refine and update their guidelines,¹ researchers to develop better means of studying airborne pathogens,² and civil engineers and architects to find innovative means of making indoor air safer while keeping energy conservation in mind.³

Although comprehensive guidelines and standardized means are available to study chemical pollutants in indoor air;⁴ there remains a general lack of suitable experimental facilities and standardized protocols to quantitatively assess the survival of pathogens in indoor air and to document their removal and inactivation by physical and chemical means. This workshop will address these issues, among others.

SPECIFIC OBJECTIVES

The workshop’s specific objectives, therefore, are as follows:

- To provide a forum for the exchange of ideas on current research on the role of the indoor environment in general and indoor air in particular in the spread of human pathogens;

* Address correspondence to Syed A. Sattar MSc, Dip Bact, MS, PhD, Professor Emeritus of Microbiology, Faculty of Medicine, University of Ottawa, 451 Smyth Rd, Ottawa, ON, K1H 8M5, Canada.

E-mail address: ssattar@uottawa.ca.

Publication of this supplement is primarily supported by RB, Montvale, New Jersey, with additional support from MicroBioFest, a division of Microbac Laboratories, Inc., Sterling, Virginia. The City University of New York (CUNY) and the University of Ottawa, Ottawa, Canada, are academic sponsors. Editorial support was provided by Ashley O’Dunne, PhD; Shannon O’Sullivan, ELS; and Alanna Franchetti, ELS of Medergy (Yardley, PA), and funded by RB.

Conflicts of Interest: None to report.

Table 1
Workshop organizing committee and support staff

Designation	Name	Affiliation
Chair	John A. Mitchell	Wordsmith Scientific and Regulatory, LLC, 3304 Wagon Wheel Rd, Bozeman, MT 59715
Co-chair	M. Khalid Ijaz	RB, One Philips Pkwy, Montvale, NJ 07645 and Adjunct Associate Professor of Biology, Medgar Evers College of The City University of New York (CUNY), Brooklyn, New York
Secretary	Mary K. Bruch	Mary Bruch Micro Reg Inc, 23 Hamilton Terrace, Hamilton, VA 20158
Members	Absar Alum	Arizona State University, Tempe, AZ 85281
	Elizabeth (Ilze) Bruning	R&D Manager, Strategic Development & Clinical Hygiene—Germ Protection & Personal Care, RB, One Philips Pkwy, Montvale, NJ 07645
	Tony Buhr	CBR Concepts and Experimentation, 4045 Higley Rd, Ste 345, Dahlgren, VA 22448
	Delbert Harnish	Research Microbiologist, Applied Research Associates, Engineering Science Division, 430 W 5th St, Ste 700, Panama City, FL 32401
	Brian Heimbuch	Associate Division Manager/Senior Bioaerosol Scientist, Applied Research Associates, Engineering Science Division, 430 W 5th St, Ste 700, Panama City, FL 32401
	Syed A. Sattar	Professor Emeritus of Microbiology, Faculty of Medicine, University of Ottawa, Ottawa, Canada
	Alice Young	CBR Concepts and Experimentation, 4045 Higley Rd, Ste 345, Dahlgren, VA 22448
Coordinators*	Jennifer Rogers	Symposia Operations, ASTM International, 100 Barr Harbor Dr, West Conshohocken, PA 19428
	B. Milewski	Staff Responsible for Committee E35, ASTM International, 100 Barr Harbor Dr, West Conshohocken, PA 19428
Administrative assistant	Kelly Dennison	Symposia Operations, ASTM International, 100 Barr Harbor Dr, West Conshohocken, PA 19428
	Hannah Sparks	Symposia Operations, ASTM International, 100 Barr Harbor Dr, West Conshohocken, PA 19428
Recording secretaries	Kathy Baxter, Darla Goeres, Rhonda Jones, and Carol Vincent	Members, ASTM Subcommittee E35.15, ASTM International, 100 Barr Harbor Dr, West Conshohocken, PA 19428

*Mary Mikolajewski and Ellen Diegel served as coordinators for ASTM in the early stages of the workshop planning.

- To discuss experimental facilities and test protocols for the study of airborne microbial survival;
- To review available means of recovering viable microbes from indoor air;
- To propose better surrogates for the study of indoor air as a vehicle for human pathogens;
- To model microbial movements in indoor air for further improvements in the design of experimental aerobiological facilities and test protocols; and
- To review ongoing research on physical and chemical means of indoor air decontamination.

The deliberations will also focus on the development of standards for assessing indoor air decontamination technologies and government regulations for registration of products to be marketed.

SPONSORSHIP AND FINANCIAL SUPPORT

As noted, this workshop has been organized under the auspices and with the support of ASTM International. The City University of New York and the University of Ottawa (Canada) are the 2 academic sponsors of the workshop, and financial support has been provided by RB (Montvale, NJ) and Microbac (Sterling, VA). These 2 companies are also funding publication of the workshop proceedings. We gratefully acknowledge their generous support.

THE PROGRAM

The organizing committee has put together an outstanding group of speakers who will offer a comprehensive yet balanced perspective on the key issues. Table 2 lists the topics to be covered, along with the names and affiliations of the presenters.

WORKSHOP PROCEEDINGS

Elsevier (www.elsevier.com) has agreed to publish the proceedings of the workshop after peer review. Elsevier will also provide a preview of the proceedings, including the abstracts for each presentation, for release during the 2016 conference of the Association

for Professionals in Infection Control and Epidemiology. The workshop proceedings will also contain a summary of the concluding discussions.

TARGET AUDIENCE

Potential members of the audience include researchers in aerobiology, makers of air purification technologies, contract laboratories that assess air decontaminants, government regulators dealing with indoor air quality, and members of standards-setting organizations, such as ASTM International (www.astm.org) and American Society of Heating, Refrigerating, and Air-Conditioning Engineers (www.ashrae.org).

BACKGROUND ON THE TOPIC

Table 3 is a glossary of the common terms used throughout this workshop's presentations. This is included in an attempt to create a level playing field while facilitating the understanding of the subject matter by experts in fields other than environmental microbiology. However, the emphasis here is on working definitions, recognizing that efforts are needed to develop a more comprehensive glossary for broader applications in this area.

Aerobiology

Aerobiology, the study of living organisms and their components in air, became a full-fledged scientific discipline in 1964. This was followed in 1974 by the founding of the International Association of Aerobiology (<https://sites.google.com/site/aerobiologyinternational/>). The initial focus of this group was the study and movement of pollen, but microbes and other life forms were soon added to the mix with a corresponding broadening of the organization's scope (Fig 1). The microbiologic quality of indoor air comes under the rubric of aerobiology (Fig 2). This workshop will focus only on indoor air as a vehicle for human pathogens.

Table 2
Workshop presentations in chronologic order

Presentation title	Speaker name, affiliation, and relevant experience	Subject matter to be covered
Welcome Introduction, objectives, and expectation of outcome	John A. Mitchell: Wordsmith Scientific & Regulatory, Bozeman, MT Syed A. Sattar: Professor Emeritus of Microbiology, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada His research focuses on the survival of human pathogenic microbes in the environment and how their environmental spread can be interrupted with physical and chemical agents. His expertise includes aerobiology of indoor air, where he has pioneered the development of several methods to study the airborne survival of viruses and bacteria and their inactivation.	Introduction of the topic with a set of definitions, clearly defined objectives, and expected outcome of the deliberations
Assessing microbial decontamination of indoor air, with particular focus on human pathogenic viruses	Caroline Duchaine: Professor, Université Laval's Research Center, Quebec Heart & Lung Institute, Ste.-Foy, QC, Canada Her research foci include aerobiology of animal and human pathogenic microbes, sampling of air for infectious aerosols, surrogates for human pathogenic viruses, and the application of molecular approaches to the study of bioaerosols.	Approaches to the study of pathogen survival and inactivation in indoor air, with particular emphasis on quantitative methods
Spread of infectious agents in the indoor environment	Yuguo Li: Professor, Mechanical Engineering, University of Hong Kong, Pokfulam, Hong Kong He studies the impact of the built environment and aerosolized droplet evaporation-dispersion of respiratory pathogens indoors, including engineering control of aerosolized infectious agents.	Impact of the built environment and aerosolized droplet evaporation-dispersion of respiratory pathogens indoors, including engineering control of aerosolized infectious agents
Generic aspects of airborne spread of human pathogens indoors and emerging air decontamination technologies	M. Khalid Ijaz: Research Fellow, RB, Montvale, NJ, and Adjunct Associate Professor of Biology, Medgar Evers College of The City University of New York (CUNY), New York, NY His research focuses on the spread of human pathogenic microbial agents via the environment, including air, and the mitigational role of hygiene, including air decontamination.	Approaches to the study of pathogen survival and inactivation in indoor air, with particular emphasis on quantitative methods
Mathematical modeling and simulation of bacterial distribution in an aerobiology chamber using computational flow dynamics	Bahram Zargar: Postdoctoral fellow at the Department of Biochemistry, Microbiology & Immunology, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada In addition to his expertise in aerobiology, his training and experience in mechanical engineering are major assets in experimental design, data analysis, and modeling of the behavior of pathogens in indoor air.	Mathematical models to predict the movement of pathogens indoors and the potential impact of air decontamination technologies
Aerobiology of the built environment—synergy between <i>Legionella</i> and fungi	Absar Alum: Assistant Professor of Research, Arizona State University, Tempe, AZ Expertise in the role of the environment in survival and spread of human pathogens.	Studies on interactions between different microbial species in biofilms in the built environment with a focus on legionellae
Knowledge gaps and future directions	Syed A. Sattar and M. Khalid Ijaz: Please see previously listed speaker descriptions.	Wrap-up with summary statements on the topics covered and a proposed agenda for research investigations, including recommendations for surrogate microbial agents
Panel discussion	All speakers	A set of preformulated questions will be presented for discussion
Vote of thanks	Joseph R. Rubino: Director of Research and Development, RB, Montvale, NJ	

Table 3
Glossary of common terms

Term	Definition	Comment
Aerosolization	Converting a liquid or powder into an aerosol; also called atomization and nebulization	Experimental aerobiology depends on equipment and techniques for safe and effective nebulization of the test microbe.
Aerobiology	Study of living organisms and their components in air	This umbrella term includes the study of indoor air quality.
Aerosols	Particles released into the air from a liquid or solid matrix	How long such particles remain suspended depends on the combined influence of the nature of the matrix, air turbulence, light, air temperature, and relative humidity.
Airborne spread	Spread of infections via inhalation of an infectious agent	Such spread requires that respirable particles carrying infectious agents remain suspended in air long enough to be inhaled by a potential host.
Allergens	Materials derived from plants (eg, pollen), fungi (eg, β -[1, 3]-glucan), bacteria or other biologic and nonbiologic sources capable of causing allergic reactions in a host	Whereas there are synthetic chemicals such as plastics capable of inducing allergic reactions, the emphasis here is on biologic materials only.
Biofilm	A slimy, multicellular layer of microbes on moist or submerged surfaces	This often is a mix of several types of microbes, including opportunistic pathogens.
Biological decay	Loss in viability of a given microbe by damage to ≥ 1 of its biologic functions	Airborne pathogens show different rates of biologic decay depending on their nature, prevailing environmental conditions, and fluid of their origin.
Chemioaction	A negative health outcome from the combined effect of a chemical and biologic agent	This phenomenon is especially relevant in aerobiology because a host is often exposed to potentially harmful biologic, chemical, or physical agents simultaneously or sequentially.
Droplet nuclei	Airborne particles derived from larger droplets after loss of water	Such droplets are crucial for the spread of infectious agents by air as their relatively small size (0.5–5.0 μm) allows for their stability in air while also permitting their retention on inhalation.
Indoor air quality	Quality of the air within buildings and other enclosures, with particular reference to the health and comfort of the occupants	The overall quality of indoor air is dependent on a mix of a variety of factors that may be site and time sensitive.
Infectious agent	A microbe capable of causing an infection	The capacity of a microbe to infect a given host depends not only on its biology but also on the general health status of the host and the portal of entry into the host.
Microbial pathogen	A microbe capable of causing localized or generalized damage to the host	Please see "Infectious agent."
Microbiome	The totality of microorganisms and their collective genetic material present in or on the human body or in another environment	A certain proportion of the microbes found in a microbiome may not be culturable but detected and identified via their genomes only.
Microbiota	A natural mix of bacteria, fungi, viruses, and protozoa in a host or an environmental niche	This term is now preferred over microflora.
Opportunistic pathogen	A microbial pathogen capable of infecting hosts whose natural defenses are compromised because of advanced age, immunosuppression, or other underlying causes	The number, variety, and health significance of such pathogens is on the rise in conjunction with the rising numbers of those debilitated by acquired or induced immunosuppression.
Pathogen (microbial)	Any microbe capable of causing damage to the host	Even an otherwise innocuous microbe can become pathogenic depending on the general resistance of the host or the microbe's entry into normally sterile areas of the body where it can become an opportunistic pathogen.
Perikairots	Environment-based opportunistic pathogens	Biofilm-based microbes such as legionellae and environmental mycobacteria can infect those debilitated because of age or underlying medical conditions.
Resident microbiota	A mix of microbes normally found in or on the host	Many members of the resident microbiota from skin and mucous surfaces are frequently found in indoor air.
Respirable particles	Particles small enough to access the alveolar space during normal breathing	Such particles may or may not contain viable microbes.
Surrogate microbe	A microbe that resembles ≥ 1 type of pathogens but is safer and easier to work with in the laboratory; also called a simulant	The use of such microbes is crucial in many aspects of microbiology, in general.
Tidal breathing	The body's automatic inhalation and exhalation process at rest	In addition to coughing and sneezing, tidal breathing can release infectious agents into the air.
Transient microbiota	Microbes temporarily acquired by a host during normal contact with the environment	

Indoor air quality

Exposure of humans to indoor air and its contents coincided with cave dwelling >200,000 years ago.⁵ Sharing of the human habitat with domesticated animals, such as cattle, dogs, and pigs, facilitated the rise of zoonotic infections, including airborne infections (eg, measles).⁶ Exposure to pathogens of humans and animals via the agency of indoor air continues to this day.

Although the focus here is on indoor air, indoor air is not entirely immune to what goes on outdoors. The air from outside an edifice affects the air indoors and vice versa. In fact, the use of fossil fuels for heating the indoors contributes directly and indirectly to overall climate change. An early consequence of energy conservation was sealed buildings and houses, which eventually gave rise

to sick building or tight building syndrome as a result of the trapping of airborne pollutants and higher levels of moisture inside.⁷

Spread of airborne pathogens indoors

Humans and animals are the main contributors of microbe-laden particles indoors. In fact, individuals leave their own personal microbial footprint as a part of the indoor microbiome.⁸ Aerosolization of microbes from biofilms and resuspension of dust are the other principal contributors to the microbial content of indoor air (Fig 3). Although the route by which airborne pathogens cause infections varies between microorganisms, improvements in the quality, quantity, and movement of indoor air can mitigate the airborne spread of many human pathogens by preventing pathogen

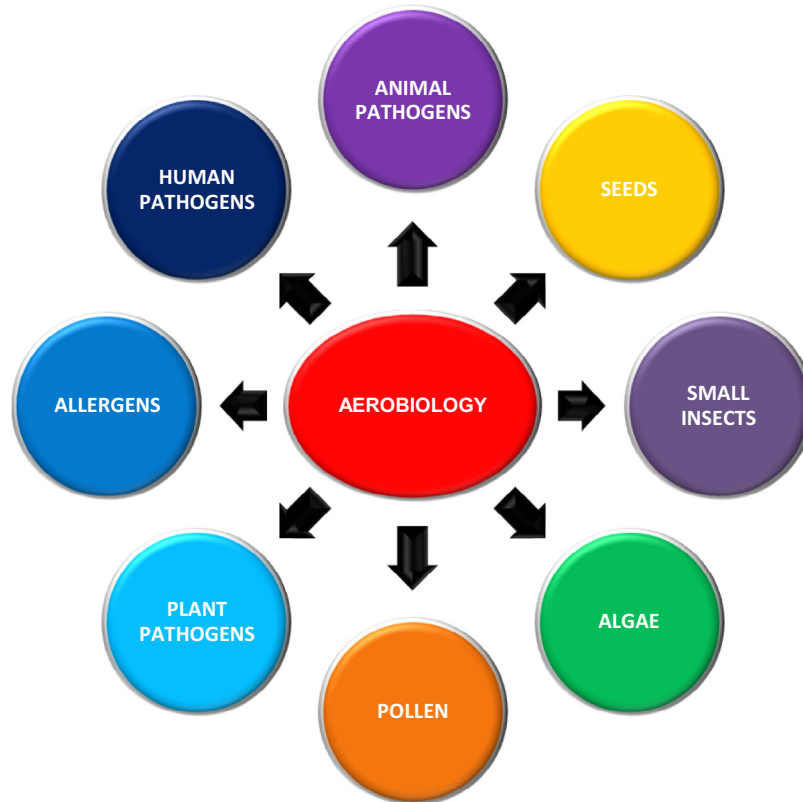


Fig 1. Components of aerobiology.

INDOOR AIR QUALITY	CHEMICAL	<ul style="list-style-type: none"> • GASES (CO, CO₂, O₃, NO) • VOLATILE ORGANIC CHEMICALS (PERFUMES, CLEANERS, DISINFECTANTS, PAINTS, PESTICIDES, OFF-GASES) • ASBESTOS
	BIOLOGICAL	<ul style="list-style-type: none"> • HUMANS • PET ANIMALS (CATS, DOGS, BIRDS) • VERMIN (MICE, COCKROACHES) • HOUSE PLANTS • MICROBES (FREE-FLOATING, BIOFILM-BASED, MYCOTOXINS) • POLLEN & ALLERGENS (ANIMAL DANDER, DUST MITES)
	PHYSICAL	<ul style="list-style-type: none"> • RADON • PARTICULATES (CIGARETTE SMOKE, PRINTERS/COPIERS) • SMOKE FROM COOKING & HEATING FUELS • DUST
	ENVIRONMENTAL	<ul style="list-style-type: none"> • OUTDOORS (WEATHER & CLIMATE) • HVAC SYSTEM • LIFE-STYLES (AIR TEMP, RH, OCCUPANT TYPE & DENSITY)

Fig 2. Factors affecting indoor air quality. HVAC, heating, ventilation, and air conditioning; RH, relative humidity.

inhalation and reducing the microbial load on environmental surfaces.

Indoor air is arguably the fastest and most highly efficient means of pathogen spread in a given setting. As depicted in Figure 2, indoor air is a complex and dynamic mixture of numerous components in a constant state of flux influenced by many factors both indoors and outdoors. The quality of indoor air represents the outcome of the unique mix of components in a given setting that, in themselves, change temporally.

One major challenge in preventing and controlling the airborne spread of infection is the presence of possibly multiple and mobile sources of pathogens at a given location and time. One or more infected or colonized persons or pets may contaminate the air in their immediate vicinity with exposure of those nearby without the air having reached any available means of pathogen decontamination.

Certain factors that influence indoor air quality may fall under the categories of chemical and physical. For example, smoke from

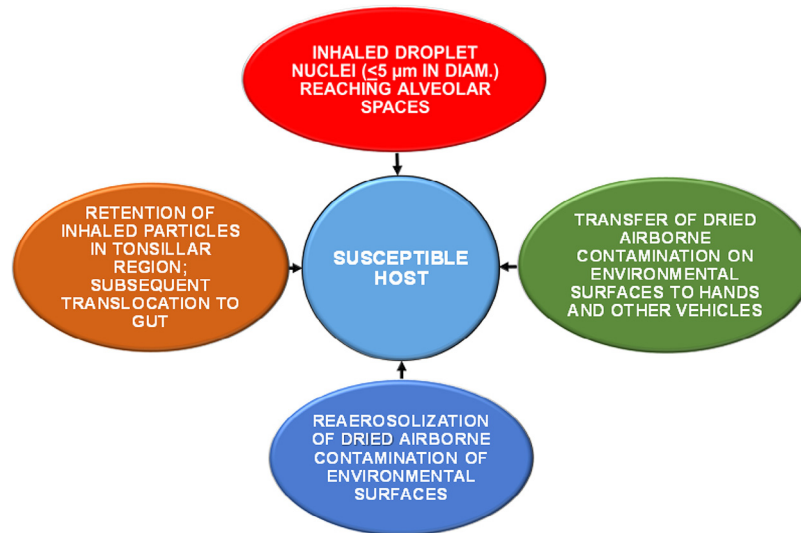


Fig 3. Airborne spread of human pathogens. DIAM., diameter.

burning wood for cooking fuel is, of course, chemical in nature, but respirable particles in the smoke are the primary means of lung irritation and potential damage leading to cardiopulmonary syndromes, including lung cancer (<http://www.who.int/mediacentre/factsheets/fs292/en/>).

The study of indoor air quality received a major boost as a consequence of the severe acute respiratory syndrome outbreak in 2003⁹ and the anthrax scares in the United States in 2011.¹⁰ It also spawned much interest in the development, assessment, and application of technologies to decontaminate indoor air.

As shown in Figure 3, particles $>10\ \mu\text{m}$ in diameter entering the air may rapidly fall out of the air because of their mass under prevailing environmental conditions, particularly temperature and relative humidity, whereas smaller particles can not only remain airborne for extended periods but can also be transported readily indoors by air currents over considerable distances. Respirable particles fall in the range of $0.2\text{--}5.0\ \mu\text{m}$ in diameter, whereas smaller particles are generally exhaled because of the aerodynamics of breathing. The actual site of retention of the inhaled particles depends on their nominal size. It is noteworthy here that persons with respiratory infections breathe out pathogen-laden particles during tidal breathing.¹¹

A human adult at rest breathes in an average of 11,000 L of air per day.¹² In any given setting, one may choose not to drink the water or eat the food that is available but generally has little choice in breathing the same air as everyone else. This makes air an environmental equalizer—conferring on it the unique potential to parse out evenly whatever it may contain. Further, infectious agents entering indoor air mix rapidly with no perceptible color or smell.

Although the potential of air to spread respiratory pathogens is well recognized, its ability to transmit enteric pathogens is not as well appreciated. Airborne particles containing enteric pathogens may be retained in the tonsillar region and swallowed for relocation to the gastrointestinal tract with subsequent replication there.¹³ Ijaz et al¹⁴ have provided a comprehensive list of human pathogens known or suspected to spread via indoor air.

WHAT TO EXPECT FROM THE WORKSHOP

The following are the main topics to be covered during the workshop.

Generic test protocols for the study of airborne pathogens under field-relevant conditions

Despite the recognized significance of indoor air as a vehicle for human pathogens, there are major gaps in our understanding of how well these pathogens remain viable under different environmental conditions. Such information is crucial to assessing the potential of a given pathogen to spread by air. Construction of an aerobiology chamber (approximately $24\ \text{m}^3$) will be described, and data from use of the chamber to test airborne survival of *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Acinetobacter baumannii* will be presented.

Assessment of newer air decontamination technologies against pathogens

Many technologies claiming microbial decontamination of indoor air are on the market, but without proper validation of their claims. Information will be presented on ways to test such technologies using standardized protocols for registration and marketing purposes.

Selection of better surrogates to study airborne human pathogens

Because they may not be readily available and generally are unsafe and difficult to culture in the laboratory, it is rarely possible to use actual field strains of human pathogens in testing. This necessitates the use of surrogate microbes to generate data predictive of the behavior of pathogens. However, certain surrogates that are used commonly and recommended by regulatory agencies and standards-setting organizations alike are inherently unsuitable for experimental work in aerobiology. For example, *K pneumoniae*, frequently used as a surrogate for airborne gram-negative bacilli, does not survive aerosolization well because it is relatively fragile and unstable in air. Therefore, data generated with *K pneumoniae* likely will not be predictive of the behavior of actual human pathogens. This workshop will identify more suitable surrogates with supporting data.

Can microbial decontamination of indoor air reduce the risk for pathogen contamination of environmental surfaces?

Data will be presented to demonstrate that reductions in the levels of airborne microbes can indeed lead to corresponding

reductions in the microbial contamination of environmental surfaces in a given setting. The use of integrated models could help analyze outbreaks, evaluate the relative importance of hygiene and infection prevention and control for policymakers, and provide guidance in environmental design for greater occupant safety and comfort. These will be illustrated using some recent examples, including severe acute respiratory syndrome, influenza, and Middle East respiratory syndrome.

Update on the recovery and quantitation of viable microbes in indoor air

Quantitative recovery of viable microbes from air is vital in aerobiologic studies. An update will be given on available methods, including their strengths and limitations.

Mathematical modeling to help better design experimental chambers for work in aerobiology

Experimentation with airborne microbes is generally quite labor intensive and costly and requires special biosafety precautions. Mathematical models can assist greatly in optimizing aerobiology chamber design and in predicting the influence of furniture and other objects on the movement of microbes. Data will be presented with specific reference to a chamber that fully conforms to guidance from the U.S. Environmental Protection Agency.

Significance of biofilms as sources of pathogens in the built environment

Biofilms are not only common in the built environment, but they can be common sources of airborne pathogens. Such biofilms often contain several microbial species having complex interactions

between them. This will be illustrated with the example of how fungi and legionellae coexist with potential risks to human health.

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