13 Indoor Bioaerosol Contaminants

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SOURCES

Bioaerosols fall into two classes: (1) airborne viable particles like fungi, bacteria, and viruses capable of multiplying under the right conditions and (2) biogenic particles like pollen, airborne antigen, and particles shed by animals and arthropods; these particles are subject to fragmentation but not independent reproduction. Bioaerosols have complex and varied organic structures; thus they differ from air pollutants (NRC, 1981). When they are present, even in small quantities, they can have very large health effects. These effects are due to infection, irritation, hypersensitivity, and inflammatory responses. Effects are characterized by human biological reactions ranging from uncomfortable to disabling (Pope et al., 1993; WHO, 1990; WHO/EURO, 1982; Lebowitz et al., 1972). Bioaerosols are both produced and concentrated in indoor environments; indoor exposure accounts for most of the attributable risk. In response, indoor bioaerosols were the focus of much research during the past decade.

A portion of indoor bioaerosols reflect natural seasonal increases, especially when growing conditions are favorable (O'Rourke et al., 1996, 1993, 1989; O'Rourke and Lebowitz, 1995; Meldrum et al., 1993). Pathogenic organisms, especially bacteria and fungi, can multiply in indoor microclimates, including ventilation systems (Pope et al., 1993; Burge, 1990; Bernstein et al., 1983). Viruses are host dependent; they do not multiply indoors but may spread among humans and from a few animal sources to humans and other animals. The airborne spread of viral disease can be facilitated by crowding of people, or through the spread of airborne virus by the ventilation system. Airborne contagion produces acute respiratory infections, which are often considered the largest single cause of morbidity (NCHS, 1988; Fox et al., 1970).

Arthropods and animals can introduce by-product aerosols that may precipitate airway hyperresponsiveness (van der Heide et al., 1997) including asthma attacks (Rosenstreich et al., 1997), and initiate a variety of allergic and irritant reactions among building occupants (RIVM, 1989; Andersen and Korsgaard, 1986). In most settings it is difficult to separate the confounding effects of multiple indoor exposures. Sporik et al. (1995) attempted this by working with school children in Los Alamos, New Maxico, where air pollution and household mite levels were low. Cat antigen loads were high in a number of homes, and asthma remained a major cause of morbidity among children (6.3%). Presence of dog in a home is associated with allergy in some, but it is rarely associated with asthma.

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Infiltration from outdoors is responsible for most indoor pollen (O'Rourke and Lebowitz, 1995, 1984; O'Rourke et al., 1989) with a negligible contribution by indoor plants. However, moist potting soil can produce abundant fungal spores. In many homes, particularly in regions with equable climates, indoor concentrations of fungi closely resemble those found outside the home with infiltration as the major spore source (Li and Kuo, 1994; Meldrum et al., 1993). Fungal concentrations become elevated in buildings where water damage has occurred and dampness is sustained (Morey, 1996; Johanning et al., 1996; Flannigan and Miller, 1994; Pope et al., 1993; Burge, 1990; Solomon and Burge, 1975). Some investigators (Ahern et al., 1995; Ezeonu et al., 1994; Rao, unpubl.) are evaluating fungal growth on various building materials. Many of these bioaerosols end up in house dust, to be resuspended with activity (Yli-Panula and Rantio-Lehtimaki, 1996; Verhoeff et al., 1994; Pope et al., 1993; Nevalainen et al., 1987).

A sizable proportion of the population has been or is capable of being sensitized (i.e., can develop a hypersensitivity) to bioaerosol contaminants over their lifetime. Allergy is thought to affect over 35 million people in the United State at some point in their lives (Pope et al., 1993). Asthma is a more dramatic disease. Death rates have risen for 0.8 per 100,000 in 1977 to 2.1 per 100,000 in 1994 (Sly and O'Donnell, 1997). The annual cost of asthma in the United States is estimated at $6.2 billion (Weiss et al., 1992). The combined effect of all bioaerosol contaminants indoors is thought to account for a substantial proportion of absenteeism in schools and workplaces, and days of restricted activity or performance. (In the general population 5 to 15 days of restricted activity per year may result; WHO, 1990; NCHS, 1988).

To understand health responses derived from bioaerosol exposures, WHO (1990) suggests evaluating (1) the species/type and nature of the suspended viable organisms or biologically derived particles; (2) the exposure to bioaerosols, including their sources, sites of multiplication, reservoirs, and means of dispersion; (3) the nature and mechanisms of the morbidity effects associated with bioaerosol exposure, including the range and distribution of sensitivity in the population; and (4) the methods of evaluation and control.

BIOLOGICAL FACTORS

In the environment, viable bioaerosols occupy three, sometimes overlapping, modalities: habitation in a reservoir, amplification, and dissemination (Burge and Freeley, 1991). Bacteria and viruses are usually brought indoors in human hosts (the major reservoir) and spread person to person (WHO, 1983a; CDC, 1987). Sometimes microorganisms become incorporated in house dust or attached to surfaces. Under the right conditions viable microorganisms reproduce, and their numbers, if not their virulence, increase. Such amplification minimizes the effects of dilution when dissemination occurs and results in the greater probability of infecting a new host. Some bacteria (e.g., *Pseudomonas*, TB) and some viruses (e.g., measles, chicken pox) can be disseminated through coughing, sneezing, and shedding of skin scales; the virus may remain as viable particles on surfaces and fabric. These particles may enter the ventilation systems (Riley, 1982; LaForce, 1986; Zeterberg, 1973), disperse, and infect other humans (Couch, 1981). Air transfer models explain most infection patterns fairly well. Recent studies also implicate direct contact among humans by hand or through fomites, or direct contact with contaminated surfaces to spread viruses like respiratory syncytial virus (RSV) (Madge et al., 1992) and influenza (Morens and Rash, 1995). Washing hands and surfaces and wearing protective gowns and gloves significantly reduced transmission of RSV, suggesting other routes of dispersal in addition to air (Madge et al., 1992).

Growth Indoors

Spores and viable bacteria are ubiquitous; they will grow virtually anywhere given the right balance of nutrient, moisture, and temperature. Specific growth requirements vary among organisms. In the indoor environment, spores and bacteria are found in house dust, which is often resuspended as bioaerosols by human or animal activity. When growth occurs, additional contaminants are produced. Bacterial endotoxins (Rix, 1997; Teeuw et al., 1994), fungal mycotoxins (Smoragiewicz et al., 1993; Hendry and Cole, 1993), and mycological volatile organic compounds (mVOCs) (Bjurman et al., 1997; Pasanen et al., 1996) may be released to further contaminate the indoor environment.

Ventilation will affect the introduction and removal, growth and control (moisture and temperature), of organisms and their resulting detritus (particles) (LaForce, 1986; Yoshizawa et al., 1987; Schata et al., 1989). Soil from indoor plants, food, and vegetal remains can support fungal growth (Raza et al., 1989). Fungal spore sizes range from 2 to 200 μm in diameter, with most spores being about 10 μm (Andersen and Korsgaard, 1986).

Moisture

Most construction materials, especially wood products, their sealants and finishes, can support microbial growth (NRC, 1981). Moisture is the major factor that promotes or limits microbial growth indoors (WHO, 1990). When the relative humidity (rh) of surfaces reaches 25%, fungal growth can occur; spore concentrations will elevate as humidity increases up to 70%. Beyond 70%, spore output does not increase (Burge, 1985) although hyphal growth may expand. Morey (1996) reports that mold will be found where rh exceeds 65% to 70% on finished surfaces. Moisture or water may penetrate into the structures, air ducts, and furnishings through diffusion, leakage, or condensation. With excess moisture the microbial growth starts immediately (Jantunen et al., 1987). This growth will lead to deterioration of building materials, which can produce more bioaerosols (NRC, 1981). Humid winter climates promote continuous problems (RIVM, 1989; Andersen and Korsgaard, 1986).

Elevated humidity indoors promotes the reproduction and expansion of mite populations inside homes. They can be found in carpets, furnishings, and fabrics where suitable nutrient (detritus) is available (Bischoff et al., 1986; Bishoff, 1989; Arlian, 1992). Mites require specific temperature and humidity regimes to thrive (Arlian, 1989, 1992; Arlian et al., 1990). Mite populations expand when indoor rh is 60% to 75% or above at temperatures of 60° to 75 °F (Arlian et al., 1982; Platts-Mills et al., 1987). Based on laboratory results, the critical equilibrium humidity for fasting *Dermatophagoides pteronyssinus* is 73% rh at 25 °C, 10 and 55% to 75% rh proportional to temperatures of 15° to 35 °C for *D. farinae* (Arlian, 1975a). Most mites die in 1 to 3 days at 40% or 50% rh, but some mites survive for 4 to 8 days (Arlian, 1975b, Arlian and Veselica, 1981, Brandt and Arlian, 1976). Since mites require relatively high humidity for survival, most surveys find the greatest mite prevalence in humid, temperate regions and the least in arid regions.

Water reservoirs associated with heating, ventilating, air conditioning, and humidification are favorable habitats for microbial growth (Burge and Freeley, 1991; Burge, 1985; Woods et al., 1989; Volk and Wheeler, 1980; WHO/EURO, 1982). Sediment collections are habitats for the bacteria, fungi, actinomycetes, algae, and amoebae. *Acinetobacter* and *Pseudomonas* have been found in cool-mist vaporizers (Volk and Wheeler, 1980; Smith, 1977). Depending on the temperature, the flora may contain thermophilic (heat-related) organisms. *Legionella* bacteria are frequently found in potable waters (WHO/EURO, 1982; WHO/EURO, 1986). Mechanical disturbance of contaminated water may produce bioaerosols; evaporation alone does not appear to do so. Very low moisture levels in air can enhance spore-release of fungi (Jantunen et al., 1987).

Ventilation

Ventilation systems serve two main functions: (1) to replace "old" dirty air with clean, "fresh" air and (2) to limit the spread of unwanted contaminants among rooms by removing pollutants from air being recycled (Seppanen, 1996). Dilution of indoor air with "fresh" outdoor air reduces the concentrations of bioaerosol contaminants circulating inside a building. Ventilation rates are generally calculated based on the floor area of a building (home) or based on the number of people expected to occupy an area (office). Seppanen reports (1996) the potential pollution load of an area plays little or no role in determining the ventilation provided to an area at the present time. Seppanen (1996) discusses air exchange rates reported by studies in several countries. In general, most studies examining air exchange in homes report mean rates of 0.3 to 0.5 air changes per hour. Mendell (1993) reviewed the ventilation literature related to sick building syndrome (SBS) in offices buildings. He reported when ventilation rates are $< 10\,L/s$ per person, there are greater complaints of SBS. Seppanen reports that in the average Finnish school, ventilation rates are $3.5\,L/s$ and well below the $6.0\,L/s$ values set by the building code. Both figures are lower than the threshold value for SBS complaints reported by Mendell (1993), and dissatisfaction abounds among headmasters at the schools (Seppanen, 1996).

Addition of outdoor air to indoor environments affects indoor humidity levels and thermal loads, and thus growth of viable outdoor contaminants. When not properly maintained, mechanical ventilation systems can become sources of bioaerosols. For example, air filters that are not routinely replaced can provide nutrients and strata for microbial growth, and handling the system increases dispersal (Yoshizawa et al., 1987; Elixmann et al., 1989; Pope et al., 1993). Air exchange in winter reduces indoor moisture and promotes the use of humidifying equipment. In summer, air exchange can increase indoor moisture, and promote the use of dehumidifiers. In sealed buildings, energy conservation measures may reduced ventilation rates, so there is an excess of human-sourced biological air contaminants (Tobin et al., 1987a,b). When there are adequate rates of airflow throughout the space, ventilation assists in drying any wet building material.

Biologically Derived Particles

Biologically derived bioaerosols consist of antigen from arthropods and their feces, especially house dust mites and cockroaches (Colten et al., 1977; Tovey et al., 1981a,b; Pope et al., 1993). Also included are fecal matter and urine from rodents, dander from humans and animals (dogs and cats), secretions, fragments or other products derived from animals and plants (i.e., horse hair, kapok), and some potential parasites from animals. Cat antigen is derived primarily from saliva deposited on fur; as it dries the saliva flakes off as particles 1 to $10\,\mu m$ in diameter; other body fluids may contribute some antigen. Dog antigen may be liberated in a similar fashion. Wood et al. (1988) found cat and dog antigen in 106 Baltimore homes regardless of whether a pet actually lived at or in the residence. Later work (Bollinger et al., 1996) compared *Fel d 1* antigen levels in 37 homes with resident cats and 40 homes lacking cats. As expected, all homes lived in by cats had detectable antigen in the air and dust sampled. Interestingly 25% of the cat-free homes had elevated levels of cat antigen in the air, and 100% of the cat-free homes had cat antigen present in the house dust, albeit in generally lower levels. Yet antigen loading in the cat-free homes was sufficient to evoke symptoms in susceptible individuals.

The composition of biologically derived particles can vary according to the production site (regional, local, microenvironmental). Biogenic particles are found in house dust, surfaces, fabrics, building materials, food, and pet enclosures. Dander and secretions from animals may be brought in from outside. Domestic mites (*Dermatophagoides spp, Blomia tropicalis, Euroglyphus maynei*, and storage mites) are widespread allergens found indoors

(Arlian et al., 1992; Kneist, 1989; Spieksma et al., 1969; Sinha and van Bronswijk, 1971). Their food source includes fungi, as well as human and other animal epidermal scales, and they are well adapted to indoor environments. Their excrement is a major proportion of the allergen in house dust (Bischoff, 1989). Mite excreta are sticky pellets about 20 μm in diameter (Tovey et al., 1981a), and the antigen contained in the pellets is water soluble (Tovey et al., 1981b) and can be found on particles less than 5 μm in diameter (Swanson et al., 1985). The humidity in the particular indoor environment is the determining feature of the species. *D. farinae* tolerates slightly lower humidity. Allergic diseases from house dust mites are most frequent in damp temperate climates. Mattresses and bedding (because of moisture from the sleeper), upholstery, and carpets (because the floor is cooler and humidity higher) are their main habitats. House dust mite antigen may be undetectable in undisturbed areas, but increase with activity (Tovey et al., 1981b). The homes of patients who have asthma associated with house dust allergy are more humid and have more mites than control homes in the same community (Tovey et al., 1981a; Korsgaard, 1983a,b).

Pollen

Both whole pollen grains and biogenic antigen particles of identical composition (airborne antigen) can be found in indoor environments (O'Rourke and Lebowitz, 1984, 1995; O'Rourke et al., 1989; Schumacher et al., 1988; Rantio-Lehtimaki et al., 1994; Yli-Panula and Rantio-Lehtimaki, 1996). The airborne antigen can be amorphous and be submicrometer in size. The submicrometer size facilitates particle penetration into the lower airways (Schumacher et al., 1988). To date over 700 homes have been sampled in the Tucson area for indoor pollen. None contain pollen attributable to house plants; a few fern spores were identified.

Most pollen found inside homes originates from outside sources. It enters the indoor environment through passive or active ventilation, on shoes, clothing, or pets. Pollen are generally spherical, oblate spheroids, or prolate. They range in size from 5 to 200 μm, though they generally are 15 to 50 μm. Most pollen settles on the floor fairly rapidly, but it can be resuspended through occupant activity. Pollen production outside is seasonal, and the quantity also varies greatly. The dominant species in any region depends on the composition of the local flora. Airborne pollen spectra vary among regions, and among years, in response to climatic variability (WHO, 1990; Holberg et al., 1987; Levetin, 1998; Rogers, 1997).

EXPOSURE

Environmental Measurement and Sampling

Sampling for bioaerosols is expensive and time-consuming. Prior to sampling, a visual inspection of the site should always be made, and obvious problems should be remediated. Only if complaints persist, should bioaerosol sampling be undertaken. Burge (1989) provided a useful approach to evaluating the workplace setting: Visually inspect the building, particularly the ventilation system, its filters, air intake, and ducts. Understanding the design and operation of the ventilation system is important. Make sure that there is an adequate supply of fresh air. Look for dampness along walls, ceilings, roofs, and in basements. Survey building users to identify special problem areas and chronic complainers. Preassessment of a building is a necessary initial phase for any investigation of SBS. Develop a sampling strategy for each room and for the ventilation system in response to symptom patterns. Choose appropriate samplers and sample consistently. Duplicate samples should be taken whenever possible, and a control, noncomplaint,

building of similar design should be simultaneously sampled along with outdoor control samples. Consider the boundary layer effects of walls and all furniture, including room dividers, when placing samplers Recommendations for remedial action must be based on clear differences among areas sampled.

The building inspection should help define the problem under investigation. Woods et al. (1989) point out some of the critical issues that must be examined prior to investigation a building. They include four essential issues: (1) determining what to measure (through consultation, qualitative, and quantitative diagnostics), (2) determining appropriate instrumentation, (3) determining how results of measurements will be interpreted, and (4) predicting appropriate building performance.

Once the problem is defined, the investigator selects the sampling equipment that best implements the study design. Bioaerosol sampling in air, in water, and from surfaces should be performed when the presence of such agents is suggested, especially when confirmation of the presence of an agent is needed or to rule out the presence of one or more specific agents (Nevalainen, 1993; WHO, 1990; Jantunen et al., 1987; Burge, 1989; NRC, 1981). In general, there are no standard methods for sampling and analysis of microbiological agents in indoor air, so it is difficult to interpret the acquired data. For collection of regional outdoor pollen and spores, the American Academy of Allergy, Asthma and Immunology has a standard protocol, but none for indoor environments. The American Conference of Governmental Industrial Hygienists (ACGIH) has developed a generic protocol for workplaces (ACGIH, 1990). Together standard protocols help establish quantitative data bases.

Sampling protocols must address the potential spatial and temporal distribution of the biological agents (NRC, 1981; Wood et al., 1989; WHO, 1990). Standard environmental questionnaires help identify factors and locations favoring growth and dispersion (Lebowitz et al., 1989a,b). Sampling has to be accompanied by detailed information concerning the site and the circumstances of collection. Spore release and pollen production are highly dependent on environmental factors, especially temperature and humidity (NRC, 1981) but also light, location, and so on. Outdoor sampling for comparisons is deemed essential. In outdoor air, seasonal variations may produce differences of several orders of magnitude. Similar problems probably exist for bacteria and their endotoxins. Therefore indoor and outdoor collections should be paired, and the building should be sampled in different seasons. Ideally air sampling should be conducted utilizing active monitors (Burge, 1989; O'Rourke and Lebowitz, 1995; O'Rourke, 1996).

Collected samples take several forms: (1) Pollen and spores can be directly deposited on slides or tapes, and impacted bioaerosols are mounted and identified morphologically using compound light microscopy. (2) Fungi and bacteria can be directly deposited on a growth media, cultured and examined using dissecting and compound microscopy. (3) Biological particles can be directly deposited on filters. The bioaerosols can be eluted, plated, and cultured, or they may be eluted and assayed using an immunological technique like ELISA. (4) Liquid impingers are used to capture bioaerosols, and the liquid is sampled and plated or examined immunochemically. (5) Samples can be collected from reservoirs of bioaerosols. This may involve collection of water from cooling towers, collection of surface wipes, or collection of dust samples. These samples may be plated directly, eluted and plated, or extracted and assayed immunochemically. Most of these collection methods rely on suction devices; some are described below. Other articles describing these samples include Ogden et al. (1974), Solomon (1988), Ausdenmoore (1988), Burge (1990), Macher et al., 1995; O'Rourke and Lebowitz (1995), and O'Rourke (1996).

In addition to the workings of air samplers, there are many important areas that bear further investigation by the novice. Many issues, ranging from the field to the lab, have entire volumes dedicated to them, and they include (1) sampler placement, (2) growth media, (3) the physics of air and samplers, (4) adhesives for particle collection, (5)

mounting media and particle stains, (6) filter characteristics, (7) elution techniques and duration, (8) choice of assay (plates, antibodies, antisera, conjugates, labels, standards, etc.), and other potential issues that may have been overlooked. Justifiable, valid choices related to these areas will make developing standardized methods for bioaerosol sampling difficult, if not impossible. At this time the equipment is fairly standard, but operational choices vary widely.

Collected air samples must adequately address the study's objectives. For instance, some collection devices rely on enumeration of intact particles. Breakage of the particles would result in inflated measurement. By contrast, immunochemical techniques quantify specific proteins incidental to the number of particles collected. One method may be better than another at addressing a specific study aim. Macher et al. (1995) provide an excellent summary of commercially available equipment, factors related to equipment operation, and equipment limitations. Sample collection is commonly achieved through impaction, impingement, filtration, and gravitational settling.

Prior to selecting a sampler, the investigator should know the aerodynamic size of the particle of interest. Then the investigator can select the sampler with the correct cutpoint and measurable particle sampling efficiency. The investigator should be careful to select a sampler best representing airborne particle concentrations (not over- or undersampling particles). Further the investigator should adhere to "good field practice" (GFP) standards for bioaerosol collection: (1) Calibration checks should be made with every use of a sampler. (2) All sampler openings should be unobstructed. (3) Sterile collection protocols with field spikes and field blanks should be employed. (4) Duplicate samples should be collected. (5) Appropriate handling and shipping conditions should be observed (e.g., cold shipment). (6) Samples should be collected under isokinetic conditions by adjusting sample suction to match air velocity.

The sample collections described by Macher et al. (1995) are used to measure the biological exposure through air. Surfaces can also be assayed. Clinical handbooks describe wipe techniques for hard surfaces. Bacteria and viruses are frequently sampled from surfaces. As an outgrowth of research related to house dust mites, researchers began evaluating dust using enzyme-linked immunosorbent assay (ELISA). Dust collection techniques are varied. Arlian et al. (1992) and O'Rourke et al. (1996) employed consistent and internally standard techniques to sample dust that complied with the recommendations of the WHO (World Health Organization) working group on house dust mites and asthma (WHO, 1986b; Platts-Mills et al., 1989). These reports recommend vacuuming a fixed area, for a fixed time, using the same vacuum in all locations used for comparison. (O'Rourke et al., 1996, vacuumed 1 m^2, for 2 minutes with a 2.2 hp Hoover Port-a-Power vacuum cleaner; dust was deposited on a filter held in special wand attachment). Dust from carpets, floors, and furniture is evaluated for a many allergens (i.e., domestic mites, cockroaches, cat, dog, and a variety of pollen and mold types) using immunochemical techniques. The approach may present a good picture of biological contaminant in the carpet reservoir, but does it accurately represent bioaerosol exposure?

O'Rourke and Lebowitz (1984) evaluated house dust for pollen content, which was abundant and strongly correlated with the regional airborne pollen of the season. Chew et al. (1996) have performed preliminary analysis of house dust for culturable fungi. Preliminary indications suggest a limited relationship between the cultured fungi and the airborne fungi by type. The most dominant carpet type, yeast, either fails to become airborne or is not readily plated from air samples. The study is ongoing and results are preliminary. Today numerous investigators are currently using immunochemical evaluation of the reservoir of biological contaminant found in house dust, and they are relating these assays to observed health effects. The extent to which a single dust measure represents a cumulative exposure requires careful consideration for each potential bioaerosol considered.

Exposure Assessment

Investigations of populations require techniques differing substantially from those appropriate for evaluating individuals. Population studies depend on reliable epidemiologic techniques, particularly the comparison of representative unbiased population samples exposed to different indoor air environments (WHO, 1983a,b; Finnegan et al., 1984).

Questionnaires are the basis for investigations (Lebowitz et al., 1989a,b). They should be validated in the community to be studied in terms of comprehensibility, reproducibility, and their power to identify the conditions under study. They should also be used to help define exposure, and to measure the major confounding factors (other factors that modify the outcome being assessed). Questionnaire responses may be altered by the method of administration and the biases of the population being studied (WHO, 1983b).

Exposure to antigenic material, either infectious agents or allergens, can be estimated by specific antibody determinations in populations. This is particularly appropriate for the study of exposure to *Legionella*, other bacteria, and viruses (WHO/EURO, 1986). It is also appropriate for the study of sensitization to aeroallergens causing rhinitis, conjunctivitis, and asthma (specific IgE and IgG estimations) and alveolitis or humidifier fever (specific IgG estimations) (Riley, 1982; Rom, 1983; Turner-Warwick, 1978; WHO/EURO, 1982; NRC, 1981; Thorn et al., 1996; Rosenstreich et al., 1997). The measurement of infectious agents can be done in the living reservoirs, human or animal (Benenson, 1985; Wilks et al., 1995). These measurements are necessary for the presence of specific agents and also for identifying sources. The quantitative assessment of exposure for individuals is probably not necessary for most agents. Isolation of *Legionella* or *Stachybotrys chartarum* from the air is a definite health hazard, regardless of how many colony forming units are detected (WHO/EURO, 1982, Johanning et al., 1996).

Exposure to allergens can be assessed by measuring airborne antigens (described above). Airborne antigen levels can be a very good measure of exposure, especially when related to time activity information (WHO, 1983a). Sufficiently good methods exists to make airborne monitoring appropriate for some important indoor allergens such as the antigens from the house dust mite *(Dermatophagoides)* (Pope et al., 1993). One should determine the presence of pets or pests and antigens they release, since they can be responsible for important contamination of indoor air with nonviable allergenic bioaerosols. The determination of sources of allergens and of exposure can be made by questionnaire or by examination of the indoor and measurements. Dampness (moisture sources and/or humidity) can be determined in all three ways. A comparison of occupants' subjective impressions of dampness with home characteristics (visible mold growth, damp stains, bugs, bad smells, wet/humid crawl spaces) and with measurements of fungi and bacteria indicate that the subjective impressions were not related to counts (van Wageningen et al., 1987).

Case studies of exposure assessment without health assessment have been provided by several groups, starting with a well-known study by Solomon and Burge (1975). Other recent studies include those on fungi (Samson, 1985; Flannigan, 1987; Strieifel et al., 1989; Ohkge et al., 1987; Jantunen et al., 1987). Humidity effects were obvious. There have been studies of fungi and bacteria (Reponen et al., 1989; Binnie, 1987; Nevalainen et al., 1987), and of other bioaerosols (RIVM, 1989; Hawthorne et al., 1989, Custovic et al., 1996). RIVM (1989) found that 15% of Dutch homes had problems with fungi and mites due to dampness. Bischoff (1989) and Colloff (1991) reviewed studies of mites (WHO, 1986b).

Most recently, Verhoeff and Burge (1997) examined results from nine residential, population based studies of fungi associated with symptom responses. Their goal was to determine risk assessment based guidelines for permissible fungi concentrations in homes.

They concluded that based on the best of the current literature, there is insufficient data to determine guidelines for permissible fungal levels. More work needs to be done with sensitized populations, using health outcomes specific for allergic disease. Appropriate aerobiological measures need to be collected in duplicate and repeated over time, and other "confounder" allergens and air pollutants should be evaluated.

The most intense health effects caused by exposure are usually found in workplaces that specialize in producing a specific product or service. Bioaerosols are a risk in certain occupations and many of the exposures occur indoors. Unlike other workplace environments, responses to bioaerosols occur after a short period of exposure, not after years. As a result workers with host susceptibility are more likely to leave the job (healthy worker syndrome) and subsequent studies of occupational health only identify subtle effects. Some occupations have known health outcomes. Farmers have long been subject respiratory diseases like "farmers lung" in response to mold (*Micropolyspora faeni*) exposures (Miadonna et al., 1994; Kokkarinen et al., 1994), and more recently "farmer's fever" (Cormier et al., 1993). Dairy farmers are more prone to chronic bronchitis than control populations when controlling for smoking (Dalphin et al., 1993; Jorna et al., 1994). Pig farmers have frequent exposure to endotoxins (Preller et al., 1995a, b, c; Dornham et al., 1995), as do solid waste handlers and processors of recycled waste (Poulsen et al., 1995a, b). Other industrial workers, such as, metalworkers exposed to bacteria (Robins et al., 1997) and fiber glass manufacturers exposed to endotoxin (Milton et al., 1995, 1996), have also contracted respiratory disease in response to bioaerosol exposure.

MORBIDITY EFFECTS

Description of Morbidity

The wide variety of biological agents and derived materials in the indoor environment are associated with a range of illnesses (NRC, 1981). The frequency and severity of these illnesses also varies by environmental and host conditions. Their contribution to total illness is quite large. However, attributable risk is not known. Of the many diseases that have been associated with contaminants indoors (NRC/NAS, 1987; Lebowitz, 1983), some are specifically associated with or caused by bioaerosols. Some of these illnesses may have other causes unrelated to the indoor environment. The size of the bioaerosol is important to potential reactions. Large bioaerosols (10–50 μm MMAD) deposit in the nose, whereas intrathoracic airway deposition occurs with smaller bioaerosols (1 to 10 μm), and terminal airway-alveoli deposition occurs most frequently for those under 1 μm (Martonen and O'Rourke, 1991, 1992).

Infectious processes (due to bacteria and viruses) include Legionnaires' disease (a pneumonia caused by the bacterium *Legionella pneumophila*), and other lower, or upper, respiratory tract illnesses. Drinking water contaminated with *Legionella* fails to cause legionellosis. Inhalation of aerosolized water containing *Legionella* is required (WHO/EURO, 1982). Currently dose-specific information for allowable levels of *Legionella* bacteria in potable water is unknown. Hospital respiratory equipment (humidifiers and nebulizers) are routinely cleaned with tap water that may be contaminated. The "cleaned" respiratory equipment may serve as a secondary source for hospital-acquired legionellosis (Woo et al., 1992). *Legionella* pneumonia accounts for less than 5% of community-acquired pneumonia but may be particular to buildings in about 30% of cases, namely hotels and hospitals (WHO/EURO, 1982). Bates et al. (1992) attempted to identify the agent(s) responsible for hospital-acquired pneumonia. They examined 198 patients with 204 cases; a direct agent was found in only half the cases. Extensive diagnostic procedures were performed on all cases. *Legionella* was the most common pathogen identified.

Four common acute or chronic local inflammatory reactions often occur together and may be produced by bioaerosols (Rom, 1983; Wasserman, 1988; Middleton et al., 1988; NRC/NAS, 1987; WHO, 1983a). These conditions may be due to infection, allergy, or nonallergic mechanisms. Rhinitis (itching, sneezing, runny, or stuffy nose) is commonly related to the indoor environment (NRC/NAS, 1987); it may be due also to dryness or coldness of the air or air pollutants. The others are conjunctivitis, (eye itching, soreness, watering, or discharge), sinusitis (pain or fullness in the face, possibly headache), and otitis (in the external or internal ear, which may cause pain and impair hearing). Allergy will be defined as a physiological event mediated via a variety of immunological mechanisms induced by specific allergens (WHO, 1990; Weill and Turner-Warwick, 1981; Rom, 1983; Wasserman, 1988; Middleton et al., 1988; Ring and Burg, 1986). Pseudoallergic reactions may be similar physiological reactions but without immunological specificity. They may be caused by direct release of mediators, complement activation, enzyme defects, or psychoneurogenic effects (Ring, 1993).

Asthma (variable airways obstruction) may be precipitated by bioaerosols. Most affected patients have multiple trigger factors (e.g., exercise and cold air, air pollutant irritants, allergens and infections). Indoor-related asthma symptoms may deteriorate within minutes or hours of exposure and improve after leaving the site of exposure. It may occur or reoccur 6 to 12 hours after exposure to an allergic stimulus (the late phase of dual phase asthma), which can occur due to indoor-related (or occupational) allergens; house dust is a good example of such a stimulus (Weinberger, 1992; Wasserman, 1988; Booij-Noord et al., 1971). Bronchopulmonary aspergillosis is a rare, complicated, specific form of asthma due to allergy to the fungus *Aspergillus* (Mrouch and Spock, 1994, Amitani et al., 1995). The same fungus may cause rhinitis and alveolitis (pneumonitis) (Malmburg et al., 1993), may produce mycetomas, fungal balls (Aspergilloma; also see Yoshida et al., 1992, for *Penicillium decumbens* fungal balls), and may be invasive in immunocompromised patients (Crissley et al., 1995; Kauffman, 1996).

Alveolitis (inflammation of the air sacs) results in breathlessness. It may be caused by nonspecific mechanisms, but indoor bioaerosols only are associated with allergic alveolitis (or hypersensitivity pneumonitis-HP)(de Hoyas et al., 1993). Most HP is caused by contaminated humidifiers (Reed et al., 1983), containing many fungi and bacteria, possibly amoebae, mostly soluble products rather than single whole organisms. The most well-known agents are thermophilic bacilli (e.g., actinomycetes) (WHO, 1990). HP is the most common illness from exposure to bird antigens, in their fecal matter (Weinberger, 1992). Pigeon fanciers can have a other immune system responses to the bird antigens (Rodriguez de Castro et al., 1993; Hasani et al., 1992). The problem is more serious since pulmonary fibrosis can occur before diagnosis. Humidifier fever is an influenzalike illness developing shortly after exposure to aerosols from microbiologically contaminated humidifiers. Recovery can occur within days, even with continuing exposure. It often occurs on the first day of re-exposure after a break from exposure. Although antibodies have been found to certain organisms, endotoxins are suspected to be the dominant cause (WHO, 1990). Experimental exposure of symptomatic workers to humidifier antigens can induce headache, rhinitis, and lethargy, as well as asthma and alveolitis; similar exposures do not cause symptoms in previously unexposed individuals. Organic dust toxic syndrome (ODTS) occurs in response to exposure to inhalation of dusts derived from products like cotton, grain, mulch, and wood chips. Wintermeyer et al. (1997) report some of the immune system changes that may be in response to endotoxin exposure.

Mycotoxicosos is an acute toxic response to products from certain molds. It is marked mostly by fatigue and irritability, and subtle alterations in immune function. There are many mycotoxin producing species that need to be considered (Jarvis, 1986; Samson, 1985; Croft et al., 1986; Flannigan, 1987; Tobin et al., 1987b; Sorenson et al., 1987; WHO, 1990). Perhaps the mycotoxin of greatest concern today is Satratoxin derived from

Stachybotrys chartarum (atra). This fungus grows under very wet conditions. It is mostly found in water-damaged buildings and prefers growing on high cellulose material. Spores rarely become airborne, so it is not routinely detected in air samples. Johanning et al. (1996) evaluated office workers who had been exposed to the fungi and toxin. They reported impairment to the respiratory and central nervous systems of some workers who experienced prolonged exposure. Mycotoxin exposure is very difficult to diagnose.

There are also skin conditions also associated with bioaerosols: Contact dermatitis (an acute or chronic inflammation) is caused by allergic, toxic, or irritant effects, from both physical contact (including constituents from flowers) and aerosols (Benezra et al., 1985; Lovell, 1993). Atopic eczema (chronic relapsing itching skin rash) commonly occurs first in infancy or early childhood, and it is sometimes aggravated by bioaerosols. Perspiration with high ambient temperatures may increase eczema as well. Contact urticaria (acute or chronic skin rash with itching) has allergic and nonallergic causes (Middleton et al., 1988).

Finally there is the sick building syndrome. It consists of a number of symptoms that are common in the general population but may, in a temporal sense, be related to a particular building. A substantial increase in the prevalence of the symptoms above background levels provides the link between the building and its occupants (WHO, 1983b; Woods et al., 1989; Redlich et al., 1997). The main symptoms are eye, nose, and throat irritation (WHO, 1986); sensation of dry mucous membranes; skin erythema; mental fatigue, headaches, nausea, and dizziness; high frequency of airway infection and cough; and hoarseness, wheezing, and unspecified hypersensitivity. There appear to be multiple causes of sick building syndrome. It has been related epidemiologically to sealed buildings, increased temperature and dust levels, environmental tobacco smoke, and psychogenic or social factors. There is also a likely role for bioaerosols, though mostly for true building-related illness (WHO, 1986; Woods et al., 1989; Wessen and Schoeps, 1996; Jarvis et al., 1996). There is epidemiological evidence that buildings with humidifiers and chillers have more symptomatic workers than buildings without, and that very dry air (< 30% RH), which is common during the heating season in very cold climates, increases many sick building symptoms (Reinikainen et al., 1988).

Health Hazards Related to Infection

The risk associated with exposure to infectious agents is determined by a number of factors to the pathogenic agents, to their exposure in the indoor environment, and to host-specific factors (Benezra et al., 1985; Fox et al., 1970). Dose–response relationships do exist. However, threshold infectious doses are not known for most viable agents. Thus the presence of pathogenic bacterial or viral species in the indoor air constitutes a health hazard per se. Emission of viruses depends on human behavior (sneezing, emission of droplets during talking, etc.) (Riley, 1982; Benenson, 1985). Droplet nuclei are 0.5 to 5.0 μm in diameter (Knight et al., 1980).

Transmission efficiency depends on the location of sources with respect to receptors. Transmission is further affected by mechanical reservoirs, air-cleaning systems, and air circulation. Other suspended aerosols can be efficient carriers of microbes. Temperature and humidity influence transmission by altering particle size, thus affecting their settling time (Benenson, 1985; Fox et al., 1970). At humidity levels higher than 65%, the incidence of upper respiratory illness can increase, and have adverse effects in asthmatics and allergics (WHO, 1990).

Some microbiological agents enter the indoor environment as diseases of pets (e.g., toxoplasmosis in cats or rabbits, psittacosis in birds), which may be transmitted (by handling) to humans. There are some animal viruses (e.g., cat leukemia virus) that may be transmittable as well, but there is insufficient information about such viruses (Benenson, 1985).

Individual susceptibility to infections is most important in determining the actual risk of developing (Rom, 1983; Turner-Warwick, 1978; Wasserman, 1988; Tobin et al., 1987a,b). Infancy, early childhood, and old age are associated with increased susceptibility. It may be increased due to various conditions — including existing disease, such as chronic lung disease; immunosuppression, as occurring under drug therapy, or during certain diseases (e.g., cancer, AIDS, other chronic affections); smoking habits and alcohol consumption, diet (i.e., low in necessary nutrients, vitamins, and minerals); occupational or ambient exposure to airway irritants which may damage the pulmonary defensive system (mucociliary cells, macrophages, etc.) — and with warm temperatures. Human susceptibility to infections decreases as a result of immunization (CDC, 1987).

Health Hazards Related to Allergens

Separate dose–response relationships exist for different populations. In a previously unsensitized population, the risk of sensitization is likely to depend on the potency of the allergen, the level of exposure, and the length of exposure (Rom, 1983; Turner-Warwick, 1978; Wasserman, 1988). Indoor air antigens vary in their potency. For example, house dust mite antigens are often considered potent, pollen relatively potent, and mold antigens less potent. Cockroach antigen may be very potent and can cause asthma, especially in inner city lower socioeconomic residents (Homberger et al., 1979; Colten et al., 1977; Rosenstreich et al., 1997; Sarpong et al., 1997).

Current evidence suggests that a considerable percentage of the population is capable of developing IgE-mediated sensitization (also referred to as *atopy*). The figure reaches around 60% of the population exposed to environmental allergens in Tucson, Arizona (Barbee et al., 1987; Sears et al., 1989). In occupational settings, this figure may be higher, reaching, for example, around 75% in biological detergent workers exposed to antigens for *Bacillus subtilis* (Turner-Warwick, 1978). Thus most of the population should be considered at potential risk for allergy. Once sensitization has developed, only a proportion will develop clinical disease related to it. Expression of disease depends on the dose, on the level of antibodies in the individual, and on nonspecific amplification mechanisms (bronchial responsiveness for asthma, releasability of mediators, skin reactivity, etc.) (Sorenson et al., 1987; NRC, 1981). Sears et al. (1989) have shown a very significant relationship between house dust and cat sensitivities with bronchial reactivity in nonasthmatics and with asthma; outdoor grass pollen had no such relationship. Di Pede et al. (personal communication) have shown similar relationships of house dust and dog to bronchial responsiveness in nonasthmatics in Tucson. In both cases IgE was implicated as the mediator.

High levels of exposure to allergens for a short period of time is likely to result in more sensitization than a similar total dose over a longer period of time. Therefore cumulative exposure is less relevant than exposure to recurrent peak levels (Turner-Warwick, 1978). Much lower doses are required to elicit disease in the sensitized individuals than to induce sensitization. Sensitized individuals that have become symptomatic often will respond similarly to other biological agents and to chemical agents, such as formaldehyde and particles, due to heightened tissue reactivity (Rom, 1983; Turner-Warwick, 1978).

Health Hazards Related to Irritants

Gram negative bacteria growing indoors can liberate endotoxins. These phospholipid-polysaccharide macromolecules are a integral part of bacterial cell walls and are water soluble. They may be distributed through the indoor environment via the ventilation system, particularly if water has seeped into the system and bacteria are growing there. Endotoxin inhalation may cause an acute illness with fever, sweating, muscle aches,

headache, and sometimes rhinitis, asthma, and breathlessness. Symptoms usually start within hours after exposure and resolve within a day. Repeated continuous exposures lead to tolerance. However, an interruption may stop symptoms, but then symptoms will start again with repeat exposure. Endotoxin exposure is a possible cause of humidifier fever and may be relevant to some of the symptoms of sick building syndrome or building-related illness (Woods et al., 1989). A substantial growth of fungi may produce mycotoxins, which in sufficient doses have potentially serious health effects. House dust may produce its effects by nonspecific irritant effects, as well as by allergy to individual components (similar to formaldehyde).

Little is known in real environments (i.e., outside of animal exposure chambers) about possible interactions between bioaerosol irritants with temperature, humidity, and other air contaminants (e.g., inorganic particulates). Lower moisture levels (below 20%) and irritants may aggravate skin diseases and produce mucosal symptoms. Some individuals may be more sensitive to these other irritants, or odors; up to 20% have eye hypersensitivity (Weber, 1984). Those individuals who are allergic often also react more strongly to irritants as well especially where their allergy manifests itself. Individuals with existing airway disease, up to 10% of the population, may have an aggravated reaction to irritants and may show bronchospastic responses.

Exposure to abnormal concentrations of spores or mycelial fragments of certain species of filamentous / toxigenic fungi or substrate particles should be considered hazardous (Jarvis, 1986; Samson, 1985; Croft et al., 1986; Flannigan, 1987; Tobin et al., 1987b; Sorenson et al., 1987). For example, inhalation of the spores of the aflatoxin-producing *Aspergillus* species from harvesting corn (grain) or groundnuts or working in processing facilities where these commodities are handled has been shown to induce the associated mycotoxicosis (liver cancer). The mycotoxins may be ingested as well, such as with *Aspergillus flavus* contaminated peanuts, indicating multimedia exposure.

HAZARD ASSESSMENT

The assessment of the effect of bioaerosols has to be made for individuals (for diagnoses and medical management) and for populations. Hazard assessment is made for populations. It is complicated by the varied biological processes that may result from exposure, separately or jointly, by antigen and irritant challenges (NRS, 1981). Some questionnaire responses are capable of validation under field conditions, such as lung function tests (with and without challenges) to validate asthma (Lebowitz, 1982). Some responses are not easily capable of validation, such as lethargy and headache. Daily diaries of symptoms can be used as well to document longitudinal and time-specific responses in relation to exposures (WHO, 1983b) The health hazard assessments differ sufficiently with the different mechanisms (allergic, infective, or irritant / toxic), and they will be discussed separately.

Hazard Assessment for Infectious Responses

Immunity toward some infectious agents can be measured by serum immunological tests, which determine the specific antibody titer, or skin tests assessing the cell-mediated immune response. Accuracy of the methods is very important, especially if such testing leads to probability distributions of immunity in populations (Fox et al., 1970). (The detection of serum antibodies against *Legionella pneumophila* is of value in the diagnosis of legionellosis in patients, but its significance as an indicator of immunity in healthy individuals is unknown (WHO / EURO, 1982).

Significant exposure to indoor infectious agents should be suspected when (1) there are several important sources, (2) there are amplifiers or conditions favoring the micro-

organism survival, (3) there are highly susceptible individuals or known carriers, (4) there are complaints or epidemics of diseases, or (5) a microbiological laboratory reports many positive cultures or high rates of seropositivity. Also buildings with high occupant densities have an increased risk of airborne transmission of infectious diseases, especially during endemic seasons.

A classic study was performed by Riley and colleagues (1959, 1962) on tuberculosis. They evaluated air vented from a TB ward into exposure chambers. The guinea pigs exposed were previously tuberculin negative but became positive after exposure, indicating infection. This was confirmed by a study on a submarine (Houk et al., 1968) in which one seaman with active TB exposed other seamen for six months. The submarine, of course, used recirculated air. Of 308 seamen, 140 became infected. Since few had direct contact with the index case, it demonstrated the infectivity of circulated droplet nuclei. Many other studies since have documented such infectious routes (Riley, 1982).

Fungal infections can lead to serious disease, as demonstrated by Staib and colleagues (1987). In HIV positive cases, they found a 3.6% prevalence rate of crytococcosis. All had been exposed to the fecal matter of caged birds or feral pigeons. In two of the cases, the isolates from sputum and cerebrospinal fluid were identical biochemically with isolates from the fecal matter of the birds to which they were known to be exposed. These investigators also isolated the same species of *Aspergillus* and Mucoraceae from hospitalized cases and from both the soil of potted plants and surrounding air.

Epidemic mathematical models help describe the spread of viruses through susceptible populations. The accuracy of such models is a function of the characteristics and size of the target population, the place and time models have been developed for tuberculosis, measles, varicella, rubella, pseudomonas, and staphylococcus. They take into account their viability in and out of the human reservoir, their passage (e.g., atmospherically, as fomites, through ventilation systems), their incubation period, pathogenicity, and virulence. Epidemic models of tuberculosis risk (spread within populations) have been better defined in general and have been discussed for indoor environments (Lebowitz et al., 1972). TB occurs about 10 times more frequently than legionellosis. Epidemic models have been discussed for certain outbreaks of legionellosis, but it does not occur frequently enough for general health hazard assessment. The other models have not been specified for different types of buildings, although attack rates and spread are more population oriented than they are building oriented (Lebowitz et al., 1972). The models are in the form of compound epidemic curves, which continue to be compounded by the influx of new susceptibles. Thus each model has parameters determined by the exposure, time, and the proportion of susceptibles. These compound distributions can represent the risk assessment exposure–response relationships; they can be defined for different populations. The risk assessment models for different indoor settings in different populations should be defined for risk management.

Hazard Assessment for Allergic Responses

Sensitization to allergens can be measured by finding specific IgE antibodies in the population, by finding positive allergy skin tests to the allergens, by finding IgG precipitins or immunoflourescent antigen-antibody reactions to the allergens, and especially by challenging the nose and airways with the allergen and measuring the response (Rom, 1983; Turner-Warwick, 1978; Middleton et al., 1988; Weill and Turner-Warwick, 1981). For example, precipitins to avian protein, especially as it waxes and wanes with symptomatology, are indicative of sensitization. As shown for HP, bronchoalveolar lavages may be useful; higher proportions of Tiells, low helper to suppresser Tiell ratios, and increased mast cells (2 + %) are indicative of allergic response (Turner-Warwick, 1978).

Responses to aeroallergens can be determined by symptoms, increased bronchial responsiveness using peak flows, increased medication use, visits to physicians or emergency rooms, and / or hospitalization. The techniques are highlighted in the studies discussed.

Fungal Reactions

Nevalainen and colleagues (1987) have reported more allergic symptomatology in occupants with elevated fungal levels, but challenge tests and other causes were not evaluated. In contrast, Licorish et al. (1985) challenged mildly asthmatic subjects and provoked asthma attacks using spores of *Alternaria* and *Penicillium* at concentrations found in doses that subjects could encounter in natural settings.

Schata and colleagues (1989) performed an experimental study with fungal antigens. They studied 150 patients, aged 32 to 47, with allergic diseases whose symptoms were reported to occur after exposure in air-conditioned rooms. (A previous report stated that 38% of allergic patients were sensitive to fungi.) The antigen extracts included 14 fungal species; they removed the mycotoxins. The extracts were used for skin tests and challenges. Four percent reacted to the control skin test, and between 11% and 73% had skin test positive results for fungi. The three most reactive antigens were all to *Penicillium* (62–73%), 13% to 51% reacted to seven *Aspergillus* species (of which *A. niger* was the highest), 47% reacted to *Cladosporium*, and 32% to *Alternaria*. However, the ultimate test, the challenge, yielded a maximum of 36% reactivity, confirming that skin test responses are not equivalent to allergic disease (but only predisposition). (The rank orders were the same for the two types of tests.) Thus, with both sets of results, one sees that sensitivity and specificity of allergic complaints are not optimum. However, desensitization for up to three years reportedly removed symptoms in 76% of patients who underwent the treatment. Others estimate that the incidence of asthma and rhinitis produced by fungi among allergics is 5% to 29% (Prince and Meyer, 1976).

Woods et al. (1989) reported a study of allergic respiratory disease, with episodes of fever, cough, and chest tightness in a workplace. The index case had a positive serology to *Aureobasidium pullulans*, a common fungus. As others complained during summer, they hypothesized that this fungus produced disease, amplified by humid conditions. Airborne fungi air sampling indicated the presence of several fungi, in descending rank order: *Aureobasidium, Cladosporium, Alternaria, Aspergillus niger*; outdoors, the order was: *Cladosporium, Alternaria, Penicillium, Aspergillus*. They concluded that *Aureobasidium* was amplified indoors, and analysis of stagnant water in fan coil drain pans showed heavy contamination of the unit by *Aureobasidium*. Thus they concluded that this was the allergic cause. However, challenge tests were not performed on occupants.

Mite, Cockroach, Cat, and Dog Reactions

Voorhorst (1967) had shown that allergic and atopic asthmatics, with specific hypersensitization to house dust mite, had clinic visits that correlated very well with mite growth curves in homes. This has been confirmed by others (Andersen and Korsgaard, 1986; Tovey et al., 1981a,b). Korsgaard (1983a) compared the occurrence of house dust mites in homes of 25 mite-specific asthmatics and 75 controls (same sex, age, and family size). The homes with asthmatics had much higher mean levels of mites (490 vs. 1 per gram mattress dust) with a clear dose–response curve. Clark and colleagues (1976) found a reduction in peak flows of children with asthma associated with house dust when house-cleaning increased particle concentration in the air; specifically, the relation was with particles less than 2 μm. Clinical improvement in patients was seen when they were removed from their homes, either to high altitude (Verveloet et al., 1979) or kept in the hospital (Platts-Mills et al., 1982). In the latter study, 7 adult patients in the hospital for

2 months showed a 47% increase in peak flow and a tenfold decrease in histamine reactivity. However, trying to change mites in houses through moisture control in one study (Korsgaard, 1983b) has not been beneficial.

Chan-Yeung et al. (1995) recruited 120 asthmatic subjects and evaluated them for the severity of their reactions to 13 common allergens. They collected seasonal dust samples from each of the homes. There was no relationship between skin test reactivity and the levels of the cat and mite allergens. However, among mite positive children daily symptom scores were elevated and peak flow scores declined. The relationship did not hold true for adults.

Rosenstreich et al. (1997) examined the role of cockroach allergy with exposure and morbidity among children with asthma who lived in 8 innercity areas in the northeast quarter of the United States; 476 asthmatic children were recruited. Skin test reactivity was recorded for specific indoor allergens (cockroach: 36.8%; mite: 34.9%; cat: 22.7%), and house dust was collected and evaluated for allergen content. High dust allergen levels were found in 50.2% for cockroach, 9.7% for house dust, and 12.6% for cat. Children with cockroach-specific skin tests who lived in highly contaminated environments experienced three times the rate of hospitalization when compared with other children. Similar results were not found among children with cat and mite skin test response.

By contrast, Sporik et al. (1995) and Platts-Mills et al. (1995) recruited 57 asthmatic children from the "perfect" high-altitude (about 7200 ft) town of Los Alamos, New Mexico. The area was considered a perfect study site because outdoor air was generally free of pollution/particulate, and there was a low probability of elevated mite and roach infestation in homes, thus limiting causal agents for asthma attacks. Pets were the dominant indoor contaminant, and allergen was found in homes in sufficient amounts to cause sensitization and the associated risk of asthma. Asthma remained a major cause of morbidity. They conclude that the specific antigen to which a person becomes sensitized is incidental. Rather it is the sensitization in conjunction with other factors that lead to the disease. They hypothesize that changes in housing conditions are driving the disease increase. Other lifestyle changes may also play a role (Platts-Mills and Pollart Squillace, 1997).

Pneumonitis/Alveolitis and Humidifier Fever

Hypersensitivity pneumonitis (HP), or allergic alveolitis, can be appraised also by other immunological tests, mostly IgG related, and inhalation challenge tests. HP has been found in occupational settings where workers are exposed to isocynates (Baur, 1995), wood dust (Halpin et al., 1994), and shell dust (Mitani et al., 1995). HP has further been shown in studies to be due to contaminated air conditioners, heating systems (Banaszek et al., 1970; Fink et al., 1971; Reed et al., 1983), and humidifiers (Burke et al., 1977). Reed and colleagues (1983) studied and outbreak of HP. They used antiserum from affected workers to test slime from a spray wash air-conditioning system. It contained antigens that reacted with the IgG antibodies from the workers. These antigens also produced positive inhalation challenge tests. They also found the antigens in the air through immunochemical procedures.

Humidifier fever (HF) has been studied in a similar fashion. Malmon et al. (1993) studied 28 workers from a small print shop. A contaminated humidifier contained fungi, amoebae, and endotoxin producing gram negative bacteria. Serological tests showed positive responses to extracts from the humidifier, but the specific agent was never identified although the endotoxins were suspected. Finnegan and colleagues (1987) studied 25 workers with HF and 90 workmates. They found positive immunofluorescent antibodies and precipitin reactions to the antigens of amoebae found in four different contaminated humidifiers; the two techniques correlated well. However, positive results did not correlate with the HF^- or work-related symptoms. Extracts from contaminated

water can produce HF by inhalation challenge, but the exact cause is unknown still; the agent could be a bacillus, an endotoxin, or an amoebae. Prevalence studies of SBS/building-related illnesses have found fungal-related illnesses of various kinds (Finnegan et al., 1984; Morey, 1989; Andersen and Korsgaard, 1986); only some of them were specific enough to indicate allergic disease (as defined).

Hazard Assessment for Irritants, Toxic Responses, and Combined Effects

Such assessment follows the protocols for other irritants, specifically indoor air pollutants (WHO, 1989, 1990). These methods are well developed; they are discussed elsewhere (Lebowitz, 1981). Physiological effects from irritants have to be distinguished from effects of temperature and humidity (NRC, 1981) and other irritants.

Experimental and epidemiological studies have been used to evaluate toxicological effects. For example, trichothecene toxicosis has been explored (Croft et al., 1986). Bacterial endotoxin from organic dust has been experimentally studied by Rylander and colleagues (1989). Their last study exposed 77 naive subjects to endotoxin (isolated or attached to bacterial cells) from *Enterobacter agglomerans* (a major bacteria found in many organic dusts). The major physiological effect was a dose-related decrease in diffusing capacity. It was accompanied by a smaller decrease in spirometry, fever, and subjective feelings of chest tightness. Some bronchial reactivity occurred after four hours of exposure. The results support epidemiological studies showing endotoxin-produced acute reactions seen after exposure to many organic dusts.

Mixed Effects from Combined Exposures

A study in Edinburgh (Strachan, 1988) reported over 3.7 times more wheeze in children where molds in the bedroom were reported, but there was no relationship to actual bronchial lability. This indicates probable overreporting bias, which is strengthened by the extremely high rate of wheeze reported in positive homes (over 38%).

An epidemiological study of the respiratory effects of dampness and mold was conducted in the Netherlands in 210 houses (202 children and 328 parents) using A WHO CNSLD questionnaire, an environmental questionnaire, and monitoring in 36 houses (van Wageningen et al., 1987). The health questionnaire yielded prevalence rates of symptoms and potential confounders. The environmental questionnaire had questions about dampness (see above) and potential confounders. Fungal spores were measured in 25 "damp" and 11 "dry" houses using modified Andersen samplers, and bacterial concentrations (using agar plates with the same samplers). Comparisons were made with symptom responses in homes with sampling but without questions about dampness. The latter substudy indicated serious reporting bias (overreporting) when dampness questions are asked: Odds ratios for symptoms, comparing prevalence rates in damp vs. dry subjects, with such questions were over 3 (3.4 – 19.1) for many symptoms, while without such questions being asked (i.e., in children) they were only 1.7 to 2.9 and significant only for cough and total CNSLD (a combination of symptoms). Further the odds ratios were often greater using the subjective "dampness" compared to the moisture index. The odds ratios were higher for those exposed to environmental tobacco smoke. An attempt to avoid such biases must be made by utilizing more objective health and exposure data without subjective data. This was confirmed by the lack of significant correlation between the moisture index and both fungal and bacterial data, especially the latter. No relation of symptoms to bacteria were found, and direct fungal-symptom relations were not presented. The authors thought that unmeasured house dust mites might be related to the symptoms; if so, they were not as related as shown in patient studies, nor to the allergic-asthma symptoms expected by mite exposures in children (Sears et al., 1989).

A major study of home dampness and symptoms in children was performed in six U.S. cities (Brunekreef et al., 1989). Similar questions were asked to detect dampness; questions were also asked about water in the basement. Nine symptom rates were adjusted for age, sex, parental education, and smoking by city. The dampness index ranged from 45.7% to 58.2%. Adjusted odds ratios were almost always significantly greater than 1.0 for molds and for "dampness" and were usually greater than the unadjusted odds ratios. (Symptoms were highly intercorrelated.) However, only cough was significantly greater in asthmatics, and all symptoms except chest illnesses were significantly greater in nonasthmatic nonwheezers. Spirometric differences were not impressive. Unfortunately, no bioaerosols were actually measured, no relation to indoor humidity was presented, and no joint analyses with other indoor air pollutants were reported (although previous analyses in this population showed effects of passive smoking and possibly nitrogen dioxide). A later abstract (Su et al., 1989) reported that total colony-forming units, derived from Andersen samplers and cultures in 250 of these homes in three of the cities, did not relate to indoor humidity or temperature; they were higher in gas-cooking homes. Preliminary results did not show correlations between CFUs and symptoms, though case-by-case analysis showed trends.

A study in England of 200 children reported relations between respiratory illnesses and bedroom humidity, nitrogen dioxide, and some effects of passive smoking (Melia et al., 1982). Attributable and combined risks were not presented, and bioaerosols were not measured. Other confounding factors were controlled in analyses.

A study of 117 asthmatic and nonasthmatic families (229 subjects) from a representative community population sample in Tucson was monitored over a three-year period using daily diaries and peak flows (Lebowitz et al., 1982, 1985). Simultaneous microindoor and outdoor monitoring was conducted in a representative sample of houses for air pollutants, pollen, fungi, algae, and climate. Macromonitoring of air pollutants and pollen was conducted simultaneously. The relationship of indoor to outdoor and micro to macro factors can be demonstrated from this study. Suspended particulate matter and pollen independently were related to symptoms in asthmatics and nonasthmatics. The use of gas stoves was qualitatively related to symptoms. Fungi were not related to symptoms or peak flow after accounting for the other environmental factors. Algae, and other contaminants of evaporative coolers, did not appear to be important in producing symptoms. *Bacillus* species found in cooler water were not related to immunological tests in occupants.

Factor-based scales, which are climate and season specific, are developed for the environmental variables (Holberg et al., 1987). Three pollutant / meteorological scales represent summer, winter, and humidity. Four pollen scales represent early and late spring, summer, and fall pollen types. Relationships among the environmental variables, respiratory symptoms, and peak expiratory flow are analyzed with path diagrams, after accounting for age, sex, smoking habits, and stove type. The different effects of the environment on asthmatics, allergics, and airways obstructive disease (AOD) subjects were demonstrated. The pollutant and meteorological variables are related to respiratory symptoms and peak flow directly, as well as through interactions with pollen types, specifically rhinitis and attacks of wheezing in asthmatics, and the attack and decreased peak flow in subjects with AOD. Some of the largest positive coefficients are seen in association with seasonal pollen types, specifically rhinitis in allergics. Micropollen was significantly related to peak flow decrements in asthmatics.

A time-series analysis was utilized to evaluate the respiratory responses to outdoor and indoor air pollutant and aeroallergen exposures in the sensitive adults (Lebowitz et al., 1987). The time-series analysis helped determine appropriate lags between environmental stimuli and health responses. Asthmatics showed that most respiratory responses, while asymptomatics showed no significant responses. Outdoor ozone, nitrogen dioxide, aeroallergens, meteorological factors, and indoor gas stoves were significantly related,

independently and interactively, with symptoms and peak flow. Pollen did not show any time lag.

O'Rourke et al. (1989) have monitored the regional/macro pollen rain in 4 representative vegetational clusters, using a Burkard 7 day pollen and spore sampler, whose tape can be analyzed by 2 hour segments. Indoor and outdoor pollen concentrations were determined in 93 households located within those clusters, using mini-Burkard samplers. Results for one spring indicate an order of magnitude difference among regional (rooftop), micro-outdoor (1.5 m above ground level), and indoor (1.5 m above floors) pollen concentrations. Based on questionnaire responses, immediate hypersensitivity skin tests, and bronchial responsiveness, 121 individuals were classified into four categories: asymptomatic, allergic, asthmatic, and symptomatic for other chronic obstructive lung disease (COLD). Individual responses were monitored with daily symptom diaries and peak flow measurements of lung function; their houses were monitored for air contaminants. (Peak flow values have been standardized based on the 2–4 daily values using the mini-Wright meter.) Analytically, multifactorial analysis of covariance is used to control for covariables and confounders in the evaluation of the effects of daily pollen and mold concentrations on daily symptom incidence and prevalence rates, and on peak flow variability. This approach evaluates the interactions of pollen and mold, meteorological and air pollutant variables, in regard to these health effects. It adjusts for other effects, whether interactions are completely additive, synergistic, or inhibitive. The regional daily mean pollen values were compared with the daily diary scores. Regional daily mean pollen concentrations reflected pollen encountered by subjects throughout the day, and the result was a compromise for exposures between pollen encountered indoors and outdoors. In contrast to "normals," "atopics" and "peak flow responsive" subjects showed increased nasal symptom responses with increased pollen concentrations.

The analysis showed a direct relationship between rhinitis and ragweed and mulberry pollen in sensitive subjects. Unfortunately, the pollen season for these two taxa was so similar that effects were undifferentiated. One may be able to differentiate these effects by assessing individuals who are allergic to specific antigens (i.e., mulberry- and ragweed-specific individuals).

The careful characterization of subjects was essential to this study. None of the "normals" showed an increase in symptom response with increased pollen prevalence. Decline in lung function, as measured by the evening peak expiratory flow, was associated with high concentrations of Morus (mulberry) pollen, but only for individuals defined as "peak flow responsive." More results will be forthcoming from this study. One can expect results in the near future from other studies with both bioaerosol and air pollution monitoring (Hawthorne et al., 1989; RIVM, 1989).

Recent work evaluates the relationship between pollen exposure and changes in peak expiratory flow. We hypothesized that persistent and elevated grass or cheno-am pollen exposures will be associated with a decline in lung function as measured by peak expiratory flow rate (PEFR). We tested this hypothesis in a previously recruited and characterized population of Pima County (Arizona) employees and their families. We visited 559 households and evaluated changes in daily respiratory symptoms, including PEFR, in over 1000 residents. Residents completed standard respiratory health questionnaires and were prick tested with *Cynodon dactylon*, *Amaranthus palmeri*, *Chenopodium alba*, and 21 other antigens and positive and negative controls. Regional daily pollen concentrations were evaluated using the Burkard 7 day regional pollen and spore sampler. Indoor and outdoor household pollen assemblages were evaluated using Burkard Personal Monitors. Daily time/activity logs were completed by subjects. From these measures, daily grass and cheno-am pollen exposures were calculated for each subject. Since daily pollen concentrations and daily lung function are both highly autocorrelated, random effect models were used to control for autoregressive factors. The

REM models can deal with irregularity in collection periods, missing data and lagged responses. We generated two types of models to examine relationships. The first model relied exclusively on local measurements of pollen inside and outside subject homes. The values collected by short-term grab samples were assumed to be stable over a 1 to 2 week period. The second model assumed that indoor / outdoor pollen ratios were stable. Variable daily pollen concentrations were reported from regional sites, and the pollen was apportioned as a function of the grab sample ratios. We controlled for gender, height, age, skin test response, and smoking behavior. Although smoking outweighs all other factors, we found a significant decline in PEFR associated with elevated grass and cheno-am pollen exposure on the preceding day during years with typical patterns of pollen production / dispersal. During nontypical years, other factors, possibly air toxics or weather conditions, confound the relationship.

CONTROLS

Strategies for the control of bioaerosols fall into two categories, those relating to the host and those relating to the physical environment. Prevention in the host can occur through immunization (for infectious agents), avoidance of sensitization (see above), allergic desensitization, and avoidance of exposures that exacerbate symptoms in the sensitized. Behavior and socioeconomic factors are very important in control. Avoidance of irritant exposures (as recommended clinically to asthmatics), including physical measures in indoor air, is predominantly based on avoiding conditions that favor bioaerosol growth. If bioaerosols succeed in growing , then the contaminants must be contained and removed. (Pope et al., 1993; NRC, 1981; WHO, 1990).

Socioeconomic Influences and Behavior

The socioeconomic conditions related to bioaerosol exposure cut both ways. Tighter buildings, recirculated air with humidifiers, deep pile carpets, overstuffed furniture, wall hangings, and heavy draperies are societal indicators of wealth. These amenities are commonly found in the homes of the middle class and wealthy. They can promote humid interiors with enhanced habitat. Once educated, the middle and upper class have the funds to remediate their environment. Generally, they will take some steps (usually modification of the ventilation system), but unless the illness is extreme, people rarely forgo comfort. Eliminating carpeting is unlikely, and removal of pets rarely happens.

By contrast those living in public housing complexes, dormitories, and rental units have control of only a small portion of their housing environment. Given appropriate education, people may effect changes in their immediate environment, but they have little or no control over their building. They have neither the means nor the power to alter the ventilation system. Residents may effectively eradicate rodents and arthropods from their units for a short period of time. Soon the vermin will return from adjacent units.

Call et al. (1993) state that "Inner city children have the highest prevalence and the highest mortality rates for asthma in the United States." They investigated homes of 122 asthmatic children (plus 22 control) in Atlanta, Georgia, for exposure to mite, cat, and cockroach allergens in dust. They demonstrated that black children in innercity Atlanta were exposed to high levels of allergen and that the combined sensitization was a major risk factor for asthma in this population. A survey in New York City (Carr et al., 1992) found that hospitalization and death rates from asthma were 3 to 5.5 time greater for African-Americans and Hispanics than for Caucasians. They concluded that there was disproportionate morbidity and mortality borne by poor and minority populations.

Behavioral controls a major determinant on the impact of indoor contamination (Pope et al., 1993; WHO, 1983a, 1986a). Modification of the behaviors that influence indoor air quality and resultant exposure often is the simplest, least expensive, and most effective means of reducing adverse health effects. For bioaerosols, these factors include a range of activities such as education, personal behavior, and social practices (WHO, 1990).

Education includes the dissemination of information to occupants on actions they could take to reduce / eliminate indoor bioaerosols and the ability to recognize situations (e.g., source and source use) that can contribute to bioaerosol concentrations. Use of the information will depend on the motivation of the individual and available resources. Individuals could use available information to reduce their exposures or remove themselves from contaminated environments in which they experience adverse health effects.

Platts-Mills and Pollart Squillace (1997) have observed a marked change in the play patterns of children over the last 30 years. Children's play used to be very active. Like adults, today's children spend leisure time watching television or playing with the computer. Lack of play with exercise eliminates the direct beneficial effect on the lung, and sitting without exercise may induce a breathing pattern that is harmful. They cite evidence suggesting that allergen exposure yields greater rates of bronchospasm with sedentary inhalation rates. They hypothesize that this change in behavior (active to passive play) allows the development of asthma in children who have become allergic to indoor allergens. Can the trend toward asthma increases be resolved by changing the play behavior of children? Will a society that is encouraging computer use by children both at home and in school now encourage a new behavior? Proposed changes in play behavior present an innovative, well-balanced, and integrated approach to resolving a disease trend.

Society can exert considerable pressure, or provide / promote incentives to control sources of contamination (NRC / NAS, 1987). In addition societal pressure can result in establishing adequate ventilation standards (ASHRAE, 1988) and ensure the institution of building maintenance practices that will minimize the potential for bioaerosol contamination. To protect the public, some governmental guidelines for reduction of biological contamination have been established in Canada (Department of National Health and Welfare, 1987). In the case of contagious diseases caused by bacteria and viruses, public health laws provide specific standards. For example, if a case of smallpox or tuberculosis is found, then standards require quarantine, source investigation, and preventive measures against further spread (CDC, 1987).

Although difficult, the financial burden associated with bioaerosols and their control should be adequately estimated. For asthma alone (regardless of attributable causal agent), costs were $6.2 billion in 1990 and are expected to exceed $14.5 billion in the year 2000 (Weiss et al., 1992; CDC, 1997). The relationship between the annual cost of heating, ventilation, and air conditioning in a given building and the annual payroll cost of the employees served is such that the annual salary costs are 100 to 200 times the total HVAC costs, when both are measured in terms of unit of floor area. This suggests that even if the HVAC costs were to be doubled in order to reduce biological (and other) indoor air contaminants, only a very minor increase in employee productivity would be required to offset such increased costs (WHO, 1990).

Physical methods

These methods of source control have been categorized into four groups by a WHO working group (WHO, 1990). Because several of these controls can have the opposite effect for other contaminants, it was stated that they should be used with caution.

Proper design and construction of buildings is the most desirable control means to avoid bioaerosol contamination from buildings and their system-related sources (NRC, 1987). The structure should consist of nondeteriorating materials so as not to offer a substrate for microbial growth. Construction materials should be chosen to effectively control moisture, which is the most important factor governing microbial growth in a building. Design should avoid the conflicts between energy conservation and effective moisture control, and where the control of one source of moisture (e.g., sealing out of rain water by a tight building envelope) will aggravate another source (e.g., moisture generated by cooking or by dense building occupancy rates). The design of the structure should allow for the removal of any condensed moisture through adequate ventilation. The construction site should be well drained.

Source modification offers several possibilities for control of biological pollution. Changes of temperature or relative humidity (two interrelated parameters) can be used to control some sources, but this will often have an opposite effect on other sources.

Maintenance, repair, and cleaning are common control strategies. They are important for moisture control, especially for *Legionella* and *Stachybotrys chartarum* (WHO/EURO, 1986; Johanning et al., 1996). In this group chemical treatment with biocides and UV irradiation have also been included, but the use of these methods should be limited because of the health risks for occupants (WHO, 1990). Keeping filters clean has been shown to be advantageous (Streifel et al., 1989).

Removal of pollutants from air can be accomplished by increasing effective ventilation and/or by air cleaning (NRC, 1987). These methods, although in principle applicable to reduce emission deriving from all sources, are in practice only of importance in few cases (Streifel et al., 1989; WHO, 1990).

These recommendations were also espoused by the Committee on the Health Effects of Indoor Allergens constituted by the Institute of Medicine (Pope et al., 1993). Other recommendations were also made by this group. They addressed issues of health care, engineering, educational programs, and the research agenda. Three important recommendations not covered above include (1) the development of an exposure assessment infrastructure that can be used by medical professional to evaluate bioaerosol contamination and causation in homes, (2) an emphasis on the role of carpets as sources and reservoirs of bioaerosols, and (3) the development of focused, appropriate, and sensitive educational materials for populations of disparate socioeconomic and educational characteristics.

SUMMARY AND CONCLUSIONS

In the past two decades there has been a major shift in the study of bioaerosols. From the 1920s through the 1970s skin test extracts focused primarily on exposures outside the home (pollen and mold). Because the outdoor environment contains such massive seasonal doses of specific allergens, physicians recommended that allergy and asthma patients avoid exposures by spending as much time indoors as possible. A few patients had problems with indoor allergens from kapok, feathers, and pets. They were encouraged to eliminate these sources. With the discovery of the house dust mite in the 1960s and the development and characterization of the allergy extract, clinicians initiated the evaluation of indoor bioaerosols in earnest during the 1980s. Immunologists and clinicians were also beginning to understand the relationships between bioaerosol exposure and asthma in the genetically susceptible, sensitized host, both in terms of development and exacerbation.

While the science of immunology was expanding its investigation of allergy and asthma, players in the world's political area found a new weapon in oil. Energy was being

used to shape political policy. Energy became more costly in the late 1970s, and engineers and contractors responded with changes in building materials (better insulation, tighter buildings) and altered designs in ventilation (lower air exchange rates). Indoor relative humidity began to climb. With greater energy costs and lower profitability, public institutions and corporate entities espoused the mantra "do more with less." Building maintenance and support of infrastructure were among the first areas cut. Unmaintained ventilation systems became sources of bioaerosols. Clinicians began seeing an elevation in asthma rate and outbreaks of respiratory diseases like Legionnaire's disease.

Concurrently a paradigm shift occurred in the field of exposure assessment. Data collected using time-activity diaries demonstrated what was known, but not thought about. People spend the majority, over 90%, of their time *indoors* (Samet and Spengler, 1991), and with energy and cost-cutting policies, contaminants in indoor air were becoming as great a health risk as contaminants in the outdoor air.

The indoor environment contains low-level persistent doses of bioaerosols posing a year-round, cumulative health hazard. In some settings (i.e., homes with cats, public housing with cockroaches) the airborne and dust loads of antigen can be extremely high and pose a real health threat to residents and their buildings. Research to define problems associated with bioaerosols and factors that promote their growth and spread has been ongoing. Today researchers, clinicians, and engineers, are identifying mitigation strategies to clean and maintain the quality of air inside our buildings.

A substantial portion of disease and disability are due to respiratory infections, allergic episodes, irritation, and inflammation from indoor bioaerosol exposure. Since these exposures are often due to building-related factors, such morbidity could be reduced significantly. Concentrations of bioaerosols indoors vary greatly in time and space. Methods for environmental sampling of bioaerosols need to be standardized to the extent possible. Only methods for pollen, specific bacteria, and viral sampling approach being "standard." Further studies on exposure and response are needed to provide useful information for risk assessment and management. These include specific programs aimed at young children.

Bioaerosols indoors are often caused by persistent moisture and/or inadequate ventilation, for which proper design, construction, and maintenance are essential in exposure prevention. Other useful controls include removal of pests and pets, plants, furnishings that provide homes for mites and other arthropoda, behavior changes, and vaccination.

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Cover Illustration The cover design uses, as a background image, an 1871 painting by Claude Monet entitled *Thames Below Westminster*. Monet was fascinated by the ever-changing light and color of the London fogs. The coal smokes that were responsible for the haze and colors were also a major source of mortality and morbidity in London at that time and for the nine decades that followed. The particularly severe fog episode from December 9 though 11 in 1873 caused close to 800 excess bronchitis deaths in London during the following four week period according to a Ministry of Health report focused on a similar fog episode of December 1952. The 1952 episode was responsible for about 1000 excess bronchitis deaths among an overall total of about 4000 excess deaths. The December 1873 episode was also cited in the January 1874 issue of *The Veterinarian*, which reported on deaths and severe respiratory distress among cattle on display at the Smithfield Club during the pollution episode. The 1954 Ministry of Health report also noted that there were once again deaths and respiratory distress among prize cattle at the annual Smithfield Club show that took place during the 1952 pollution episode. Control of coal smoke emissions in the United Kingdom after the 1952 "killer fog" has not only greatly reduced excess daily mortality, and the prevalence of chronic bronchitis, but also increased visibility and the frequency of mild sunny days.

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