

Microbiological Agents As Health Risks in Indoor Air

by Robert Burrell*

Ambient air may be contaminated with or carry significant levels of a variety of potentially harmful microorganisms. There are three major sources of such microbes: *a*) those arising from microbial decomposition of various substrates associated with particular occupations (e.g., "moldy" hay leading to hypersensitivity pneumonitis), *b*) those associated with certain types of environments (e.g., Legionnaires' bacteria in water supplies), and *c*) those stemming from infective individuals harboring a particular pathogen (e.g., tuberculosis). This presentation deals primarily with important microorganisms from occupational and environmental sources and clearly differentiates from case to case transmission via droplet nuclei infection. Microorganisms that are uniformly injurious are differentiated from those that are more opportunistic (i.e., those that cause problems only in people with preexisting debilities).

Such microorganisms are categorized according to whether they are allergenic, infectious, or capable of inducing toxic or inflammatory reactions when inhaled. Representative examples from each of these categories, which include bacteria, fungi, rickettsia, and amoebae, are discussed. The conditions responsible for the entrance of significant numbers of these microbes into the air, the mechanisms by which they produce injury, and the methods of prevention are also considered. With attention given to some of the basic sources and requirements for such microorganisms to reproduce and enter the ambient air environment, it is a relatively simple matter to prevent the occurrence of health problems.

Introduction

The purpose of this paper is to define and characterize the microbial components of indoor air by source, type of agent found in specified indoor environments, and type of adverse reaction caused by the inhalation of such agents. It is first important to realize that air is not sterile, even in highly controlled environments (e.g., the operating rooms of modern hospitals). The fungal spore concentration in outdoor air, seldom (e.g., contaminated farm building) can reach 3×10^9 spores/m³ (1). By comparison, the fungal spore content of indoor ambient air, such as that found in homes and offices, may reach a burden of only 10 to 30% of that in normal outdoor air provided that there is no additional internal source of contamination (2). The outdoor range is affected by such diverse features as temperature, relative humidity, season, amount of snow cover, and even such factors as the proximity of parks or woods to the site being sampled. Indoor air is affected by such factors as moisture, relative humidity, insulation, and maintenance of ducts and air circulation equipment, etc. Conversely, the bacterial content of indoor air may be more than that found outdoors, where ultraviolet light is bactericidal to airborne microorganisms. The concentration of indoor bacteria is affected by humidity, the number and density of humans, the amount and type of activity, and air circulation. A typical aerobic concentration of bacteria may approximate 15 to 500 colony-forming units (CFU)/m³ (3). Although no actual safety data are available, the figure of 10^3 microorganisms/m³ is generally considered the maximum safety level (4). These

imprecise data are based on numbers of living microbes, although microorganisms need not necessarily be living to be harmful.

The primary concern, however, is the quality or composition of the airborne microbial content because it is the type of specific microorganisms in the air, together with a susceptible host, that determines the morbidity of adverse reactions. While many people have the opportunity to be exposed to potentially harmful microbial aerosols, various host factors will further define whether a given individual develops a disease or reaction. This ranges all the way from virtual certainty, following exposure to such primary pathogens as measles or tuberculosis, to a very low rate or occasional incidence of disease (e.g., hypersensitivity pneumonitis or acute Legionnaires' disease). Everyone is exposed to microorganisms causing these latter illnesses, but only some become clinically ill.

Sources of Microbial Content of Indoor Air

Three sources of environmentally significant microbial contaminants of indoor air may be considered. Among the best-studied sources are those arising from microbial decomposition of various substrates associated with particular occupations (4). Table 1 lists several genera of fungi associated with the etiology of hypersensitivity pneumonitis. This entity is considered an occupational disease among those workers associated with some agricultural, woodworking, sugar cane processing, and certain other industries. In these instances microbial contamination of organic substrates, particularly by thermophilic actinomycetes,

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Table 1. Representative agents associated with hypersensitivity pneumonitis.

Active principal microbe	Source
Thermophilic actinomycetes Thermomonospora spp. Thermoactinomyces spp.	Moldy hay, mushroom, compost, bagasse, ventilation systems
Cryptostroma corticale Aspergillus spp. Penicillium spp.	Moldy maple bark Decaying vegetative matter Decaying vegetative matter, cheese making
Amoebae Naegleria spp. Acanthamoeba spp.	Humidification systems

results in the production of huge numbers of respirable hyphal fragments and spores. The same disease has also been known to occur in the white-collar office environment and results when air treatment equipment becomes contaminated with the same types of micro-organisms. In these instances the equipment is responsible for forcing the microbial components through the air ducts and then disseminating them into the office environment.

A second common source of significant microorganisms in indoor air is associated with certain types of environments (e.g., Legionnaires' bacteria or endotoxin-containing bacteria in water supplies). When water from such equipment as humidifiers becomes contaminated with appreciable numbers of these common bacteria and is aerosolized, ambient air concentrations reach levels of health significance, and infection or toxic reactions occur. In both of these sources the presence of moisture is a critical component. Like any other organism, microbes require suitable growth conditions (temperature, humidity, and growth nutrients or substrate). These conditions define the parameters of optimum growth, but some mechanism by which these microbes become airborne remains necessary. In the case of spore-forming bacteria and fungi, the growth habitat of the microbe lend itself to aerosol dispersal. Respirable-sized spores are delicately attached to microscopic structures such that when the apparatus is disturbed by even the slightest air current, the spores become airborne. Indeed, this ensures the dispersal and the continuity of the microbe as a species. At other times, microbes in water supplies or other substrates must be mechanically aerosolized to become airborne, either by equipment incidental to the growth of the microbe (e.g., air humidifiers, air conditioners, etc.) or by some occupationally related means (e.g., composting agricultural wastes, pitching moldy hay, etc.).

Finally, some microbes are capable of inciting an infectious process via the aerosol route as a source. These microbes must be differentiated into two groups. One group is composed of primary pathogens (i.e., microbes whose contact invariably leads to some degree of infection in all normal, nonimmune hosts). Some of these infections may be inapparent, as is often the case in primary tuberculosis, or obviously active as in measles or mumps. All such microbes originate from other infective individuals harboring a particular pathogen (e.g., in tuberculosis).

Although this paper is not concerned with case-to-case transmission of such uniformly pathogenic infections by respiratory droplet nuclei transmission, there exists the possibility of infection by association with either known or subclinical cases of such diseases in a closed environment. Table 2 lists some of the major primary infections that may be acquired via the aerosol route from nonhuman case sources. Environmental fac-

tors that promote the spread of such infections are poor ventilation, close quarters, lack of sterilizing sunlight, and high humidity, together with stressful conditions imposed on the host. Almost any pathogen is capable of pulmonary infection if environmental conditions are favorable. Rabies, a disease transmitted by the bite of an infected animal, can also be acquired by the respiratory route in caves with high concentrations of bats, some of which were known to be infected (8).

The second group of microbes consists of a number of opportunists (Table 3), microbes of low virulence that abound in normal environments and may even colonize tissues of normal individuals, but never cause disease as long as the individual remains healthy. These microbes become pathogenically active only when some debilitating condition lowers the normal immune responses to the point that the opportunist is no longer kept in check. Although environmental conditions are responsible for the ultimate source and numbers of these airborne microbes, it is impossible to avoid all contact with them.

Types of Microorganisms Found in Indoor Air

Microorganisms represent a very heterogeneous and extremely diverse group of entities having in common only their microscopic size. Even size may extend into the macro range among fungi, whose hyphal strands collect into large aggregations of mycelia and form gross fructifications (e.g., mushrooms). The microbes or their parts that are of concern here are those in the respirable range (6). Large particles in the 30 to 60 μm range consist of dirt or fibers on which microbes may be adsorbed; these are filtered out in the nasal cavity. Particles in the 10 to 20 μm range include many types of pollen, hyphal fragments, and smaller inert particles, which might have microbes adsorbed. This size of particle deposits on the major airways

Table 2. Primary airborne pathogens from nonhuman sources.

Agent	Disease	Source
<i>Bacillus anthracis</i>	Woolsorter's disease, pneumonic and cutaneous anthrax	Contaminated hides, bone meals, etc.
<i>Histoplasma capsulatum</i>	Histoplasmosis	Soil enriched with bird droppings
<i>Coxsiella burnetii</i>	Q fever	Contaminated meats, animal products
<i>Chlamydia psittici</i>	Ornithosis	Dried droppings from infected fowl

Table 3. Common airborne opportunistic infections.

Agent	Disease	Source
<i>Cryptococcus neoformans</i>	Cryptococcosis	Pigeon dropping contamination
Acanthamoeba spp.	Various amoebic infections	Natural water sources
Legionella spp.	Legionnaires' disease	Natural water sources
Atypical mycobacteria	Tuberculosislike illnesses	Water vegetation
Aspergillus spp.	Allergy, bronchopulmonary aspergillosis, mycetomas, hypersensitivity pneumonitis	Widespread in decaying vegetation

(i.e., the primary and secondary bronchi). Truly respirable particles are in the 1 to 5 μm range, the size of most bacteria and fungal spores. These particles are considered respirable in that they may penetrate the lung as far as the distal alveoli and respiratory bronchioles.

Fungi are unicellular (yeasts) or multicellular microorganisms consisting of long, microscopic strands of hyphae to which are attached different types of spore-forming structures (conidia). This group is exceedingly diverse, and their spore-bearing structures facilitate aerosolization without help from human activity. Bacteria are smaller, unicellular microbes that may exist singly, in pairs, aggregates, or in chains. Individually, most are in the 1 to 4 μm range and few form spores. Actinomycetes are a transitional group between the true bacteria and the true fungi, having characteristics of both (i.e., the size of bacteria, but the growth habits of fungi in their manner of hyphal and spore production). One particular group, the thermophiles, are of particular medical interest and are so named because of their optimum growth temperature in the 45 to 55°C range (7). Such temperatures are reached in composting materials where metabolic activities of initial populations of microbes result in heat as a byproduct that becomes trapped in the insulation of the composting organic matter. As temperatures rise, the initial populations are ecologically replaced by successive populations of microbes with increasingly higher optimum growth temperatures.

Protozoa are microscopic, unicellular microbes resembling animal cells (8). They have organelles of locomotion and ingestion, may be immediately responsive to environmental stimuli, etc. They may be free-living or parasitic and are very common in environmental water sources. Only one rickettsia, the etiologic agent of Q fever, is of importance here. They are obligate parasites, resembling viruses more than bacteria, devoid of conventional cell walls, yet they have ribosomes and some primitive forms of synthetic ability.

Types of Reactions Caused by Airborne Microbes

Allergy

A major type of reaction caused by the inhalation of airborne microorganisms is IgE-mediated, immediate hypersensitivity or allergy. This type of hypersensitivity is due to the presence of antigen-specific antibodies of the IgE class circulating in the blood and external body secretions. In order for these antibodies to induce allergic symptoms, they must first be bound to circulating basophils and tissue mast cells. When two or more IgE molecules are cross-linked by reacting with antigen, various pharmacologically active mediators are released that contribute to the inflammatory and allergic signs and symptoms (9).

Almost all microbial allergens are fungal in origin, with some extracellular enzymes of bacteria occasionally being important in selected environments. The major species most often incriminated are listed in Table 4. Collectively, fungal spores represent a ubiquitous source of potential allergens.

Moldy, dusty environments are exceedingly uncomfortable places for allergic individuals. The quantity of a specific airborne allergen need not be high, inasmuch as highly allergic individuals may react to extremely small concentrations of

Table 4. Common fungal allergens.

Penicillium	Epicoccum
Aspergillus	Trichoderma
Cladosporium	Pullularia
Alternaria	Ganoderma
Stemphyllium	Curvularia

antigen. Consequently, the elimination of the offending allergen is often impossible.

It is important to realize that development of an allergy is more than being exposed to the antigen and producing IgE. Everyone is exposed to some of these spores, yet only about 15% of the population is described as clinically atopic (i.e., they have the propensity to develop such signs and symptoms when exposed). These individuals possess a variety of intrinsic genetic factors that cause them to react in such an exaggerated manner. Of these clinically atopic individuals, a small percentage may actually be allergic to a specific fungus. Fungi need optimum growth conditions to survive and produce spores in large numbers. Some fungi are seasonal, responding to the presence of substrate and optimum temperature and moisture. Spore concentrations under such conditions may reach very high levels and can enter household or office environments far removed from the source of their production. Others are perennial in the sense that once the molds have grown to maturity in such places as damp basements, used-furniture stores, and old theaters, they represent a continuous source of airborne spores.

Opportunistic Infections

Airborne microbes may cause a variety of infections, including those obvious cases of person-to-person transmission diseases. One of the most infamous causes of airborne disease from an environmental source is the microbe responsible for what has become known as Legionnaires' disease. The original epidemic attributed to this disease occurred in 1976 and was notable because of its high rate of hospitalization and mortality (10). Subsequent studies not only identified a previously unknown group of microbes, but also indicated that not only was this microbe very prevalent in almost all water supplies, but that similar, though less virulent epidemics had occurred at other locations in the past. The epidemic at Philadelphia's legionnaire convention was noticed because the most serious forms of the disease occurred in older people with preexisting cardio-pulmonary diseases or other forms of compromised health. Most people are exposed to this microorganism regularly but seldom experience noticeable signs or symptoms. When symptoms do occur, they are often mild in nature.

The mycobacteria are related to the actinomycetes and contain species responsible for tuberculosis and leprosy. Although the former is certainly transmitted from active cases to susceptible hosts, ambient air would only be expected to contain viable tubercle bacilli if an infected individual were inhabiting the premises. Other less virulent species (the "atypical" mycobacteria) are associated with normal environmental sources. Although it is not clear just how man contacts these agents, it almost certainly is via the respiratory route but not from other infected cases and usually does not lead to overt disease. Overt disease is usually a result of other complicating or debilitating factors.

A variety of environmental fungi are capable of causing pulmonary infection in man and animals (11). Cryptococci are yeasts associated with environmental sources that may be picked up by the aerosol route. While in some cases they may behave as a primary pathogen, cryptococci generally considered opportunists and require preexisting debility for establishment. Cryptococci are most closely associated with soil contaminated with pigeon droppings, a substrate rich in creatinine, which enhances cryptococcal growth. Excessive contact with dried pigeon droppings should be avoided, although this microbe also can be found in the ambient air in most urban environments.

The aspergilli are mycelial fungi belonging to a large genus with a variety of ubiquitous species. The species of greatest concern are associated with decaying vegetative matter. At the end of the growing season when crops, forage, and other vegetative matter are in decline, aspergilli quickly overcome the plants' defenses and begin to cause decay. Spores are produced in large amounts, and the air burden can increase dramatically. Even indoor environments can carry appreciable burdens. Certain species can lead to a variety of diseases. They are common allergens that can be associated with simple seasonal rhinitis or may lead to a more complicated form known as bronchopulmonary aspergillosis. They can also colonize pulmonary abscesses producing mycetomas that can be confused with cavitary tuberculosis or pulmonary cancer. Finally, they may cause invasive disease in debilitated individuals.

It is becoming increasingly recognized that even protozoa may become airborne and be associated with human infection. Species of the genus *Acanthamoeba* are found in a variety of temperate, fresh water habitats. These species (and possibly those of *Naegleria*) are certainly capable of being acquired by the respiratory route in environments where contaminated water sources may become aerosolized by either natural or artificial means. When infections occur, they are largely in immunocompromised or chronically ill individuals. *Naegleria* appears to be a primary pathogen (8). The infections are serious and involve the central nervous system. Another intriguing association of these protozoa with human disease is that they can ingest the Legionnaires' bacilli, trapping them within phagocytic vacuoles. Since cysts are resistant to chlorination, this may present a way for the bacteria to escape destruction (12,13). What role this interesting phenomenon may play in clinical disease remains to be proven, although humoral antibodies to these protozoa have been found in people exposed to water contaminated with these protozoa, indicating an intimate human-protozoa exposure.

Primary Infections

An acute and often lethal disease is inhalation anthrax, fortunately very rare in the United States. Anthrax is a result of inhaling endospores and vegetative cells of the anthrax bacillus. The source of this microbe is infected hides and wools of animals from countries where anthrax is endemic and is seen in humans occupationally exposed to these products. Anthrax is a rapidly fatal disease (unless treated with antibiotics), made worse by the fact that the endospores are intensely resistant to environmental disinfectants. Once soil becomes contaminated with the spores, it becomes environmentally unsuitable for further animal or human use.

One of the most common airborne fungal infections is histoplasmosis, which is caused by the inhalation of a particular spore stage in the life cycle of the fungus. Growth and production of these spores is certainly greatly enhanced by bird and bat droppings, but soil type and alkalinity also are important. Hence, cleaning such places as roosts, belfries, and attics where birds and bats have lived and their droppings have accumulated is fraught with danger. The disease may range from inapparent to acute and may be confused with tuberculosis. There is no person-to-person transmission because the infective stage only can be produced at room temperature.

The only rickettsial disease to be concerned with from airborne sources is a disease of animals called Q fever. All other rickettsial diseases are transmitted from person-to-person by intermediate arthropod vectors. These microbes require living cells for growth and reproduction, hence they will not be found in inanimate sources. Animal and meat workers exposed to infected carcasses will almost certainly contract the disease (usually manifested by a pneumonia, although other clinical forms are known) via the respirable route.

Toxic or Inflammatory Reactions

Inhalation of microbes or their structural cell wall components may lead to a variety of inflammatory conditions of complex pathogenesis. Chief among these is hypersensitivity pneumonitis, a range of clinical entities from acute mycotoxicosis caused by the one-time inhalation of large amounts of mycelial/spore matter, to acute disease in individuals with prior sensitivity, and to progressive, lethal disease occurring in individuals with undefined intrinsic susceptibility (14). Cell walls of the representative microorganisms associated with these entities are known to incite inflammatory reactions (largely through the enzymatic cascades like the alternative complement pathway), activate macrophages, initiate lymphocyte mitogenesis, and induce specific immune cytotoxic cells. The combination of any of these specific immunologic mechanisms together with undefined host factors may lead to one of these manifestations or, indeed, to no manifestation at all (15).

It is not necessarily a prerequisite to inhale living microbes to cause adverse reactions. Activation of inflammatory cascades or elicitation of allergic reactions do not require inhalation of living agents because the response is to molecular constituents of the microbe.

It is well known that the structural components of bacteria and fungi are extremely bioactive, capable of initiating a variety of inflammatory and immunomodulatory activities. One such material is bacterial endotoxin, an integral structural component of the cell walls of Gram-negative bacteria. This substance is highly inflammatory and can activate innumerable mediator systems, giving rise to a variety of physiologic effects (16,17). Endotoxin is heat stable, ubiquitous, and capable of eliciting inflammatory reactions in extremely small concentrations. Worse, the substance has the capacity to enhance the effects of other inflammatory stimuli such that coincidental exposure to two or more incitants, including endotoxin, can possibly result in serious pulmonary injury.

Occupations in which workers are constantly exposed to endotoxin may be at risk of developing pulmonary or even systemic disease. Humidifier fever, a poorly defined reaction brought

about by inhaling humid air contaminated with significant endotoxin, is the prototype (18). A disease seen in cotton-mill workers, byssinosis, may have an endotoxin component inasmuch as disease incidence most closely correlates with airborne endotoxin levels (19). The source of the endotoxin is from the dried plant parts (bracts, sepals, etc.) that contaminate the raw cotton fibers. When these contaminants become dry and brittle they are easily aerosolized into respirable particles in the ginning and carding operations.

Studies of some of the less acute epidemics of Legionnaires' disease indicate that many victims reported symptoms only a few hours following exposure, a time much too short for an infectious disease. This gives rise to the possibility that there is also a toxic component associated with exposure to this organism (20). Although cell wall structural components of Gram-positive bacteria such as lipoteichoic acids and peptidoglycans are also known to be bioactive and inflammatory, little is known about what happens following inhalation of these substances (21).

Prevention

It is important to be cognizant of the varieties of microorganisms existing in the air that can cause human and animal illnesses. Knowledge of the life histories of these microbes is essential in identifying their source and the environmental conditions that are responsible for introducing the microbes into the air in significant numbers. Before much can be done about prevention, the pathogenic mechanisms by which these microbes cause adverse reactions must be taken into account because absolute elimination of the microbes may be either impractical or impossible. Unique host factors that may predispose an individual to developing idiosyncratic reactions to a given agent must also be considered. This is especially the case when considering an individual's extreme allergy to even small amounts of airborne spores.

Methods of prevention should be considered in the order of biologic importance (i.e., using the preventive medical dictum that it is much easier to prevent an illness than cure it). Similarly, it is much easier to prevent airborne contamination than it is to purify the air. One of the most important preventive methods is the removal of substrate in which microorganisms build up their numbers before entering the air. Proper removal and disposal of vegetative wastes is an obvious choice, but, if impractical, ways in which the moisture available for microbial decomposition of these wastes is reduced or eliminated can often be effective. Sources of unique, principal, infective microbes can be controlled by quarantine and inspection (Q fever and anthrax), or by reduction of bird roosting sites on buildings, homes, and schools (histoplasmosis and cryptococcosis). Air quality can be enhanced by periodic maintenance of air treatment and distribution equipment, prevention of leaks, chlorination of water used in humidifying systems, and giving special attention to any system or process that uses recirculating liquid and can produce an aerosol. The key thing to prevent in any environment is allowing water to contact a suitable organic substrate. Leaky roofs, walls, and equipment are often the original source of such contact that allows microbes to grow and enter the air.

Air purification methods are less satisfactory once contamination is present. Filters often are not efficient in removing microbes of respirable size. If they are, equipment and power

costs are high because of the increased pressure necessary to drive air through filters of sufficiently low porosity. Personal filtration masks of pore size sufficient to remove particles in this range are very difficult to use, especially if work requiring any degree of exertion is necessary. Controlling humidity has two sides. Low humidity is related to personal discomfort because of increased personal evaporation, but raising the humidity increases the chances for microbes to multiply and enter the system. Ultraviolet air treatment lamps work effectively under controlled laboratory conditions, but are mostly cosmetic in actual practice.

The most difficult situation to correct is that in which an individual has developed a severe reaction (e.g., bronchial asthma or hypersensitivity pneumonitis) to the presence of a particular microorganism and it is impossible to remove that agent completely from the environment, as is often the case in agricultural products industries. If elimination of the agent is impossible, the simple solution is for the individual to give up his occupation, clearly not an easy thing to accomplish. Where large groups of people are potentially exposed, other theoretical (but often impractical for social reasons) ways to control the incidence of these diseases is to prevent workers with certain clinical markers or personal traits from entering that particular job. Individuals who are clinically atopic or who demonstrate the lack of a particular enzyme inhibitor (e.g., α -antitrypsin deficiencies associated with the development of pulmonary emphysema) should not be exposed to the unavoidable presence of potentially injurious airborne contaminants.

The most important personal risk factor (and one that can be controlled) for the development of pulmonary disease following exposure to additional environmental insults is smoking. Smoking has been epidemiologically shown to substantially increase the risk of developing pulmonary disease from a variety of airborne materials (22). Another possible enhancing factor is one that has not been explored, nor can it be controlled. This is the presence of coincidental pulmonary infection at the time of exposure.

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