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INDOOR AIR POLLUTION AND INFECTIOUS DISEASES

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HISTORY

Indoor air was suspected as a potential agent for transmitting infectious disease nearly two thousand years ago by Lucretius, who saw dust motes in a sunbeam in a darkened room and considered the possibility that the motes might carry pestilences. However, many centuries passed before microorganisms were discovered and their connection to disease confirmed (Gregory 1961). It has been well documented that some diseases can be transmitted by air (National Research Council 1961, 1981; Kundsin 1980). The indoor environment can potentially place human occupants at greater risk than the outside environment because enclosed spaces can confine aerosols and allow them to build up to infectious doses (Spendlove and Fannin 1983), and ventilating systems can pick up contaminated air and distribute infectious doses of microorganisms to other parts of the building (Huddleson and Munger 1940). Components of ventilation systems can actually become contaminated with pathogenic microorganisms (e.g., *Legionella*) that are subsequently transmitted to building occupants (Glick et al. 1978; Kauffman et al. 1981).

MICROORGANISMS, DISEASES, AND INDOOR AIR

Microorganisms that have been shown to cause infectious disease by transmission in indoor air include viruses, bacteria, fungi, and protozoans. Viruses are obligate parasites restricted to living cells. Most bacteria can survive on nonliving material; in other words, they are saprophytic. Some prefer the saprophytic environment whereas others can utilize both living and nonliving substrates. Only a few are obligate parasites. Fungi, in general, are saprophytic or pathogenic for plants but

can cause infectious disease in compromised human hosts. Only a few are primarily pathogens for vertebrate animals. Protozoa are usually free-living saprophytes although some routinely colonize vertebrates and cause disease when the host's defenses against infection are compromised by drugs, disease, or other factors (Hughes 1982).

Any respiratory pathogen that can survive aerosolization and transport in air must be considered a potential cause of airborne disease. Viruses that are known to be transmitted by the airborne route include those causing influenza, measles, chickenpox, smallpox, and the common cold (Riley 1982; Solomon and Burge 1984; Ijaz et al. 1985). Diseases caused by other viruses (e.g., rabies) have been contracted via the airborne route only under highly unusual circumstances, such as exposure in heavily contaminated bat caves (Spendlove and Fannin 1983). Theoretically, many viruses, such as hepatitis B, could be contracted through exposure to the intense aerosols that can result from laboratory accidents (Petersen 1980). Bacterial diseases that have been transmitted via indoor air are Legionnaire's disease (the only bacterial disease *primarily* transmitted via the airborne route from environmental reservoirs), tuberculosis, anthrax, and brucellosis. The fungal diseases such as histoplasmosis, cryptococcosis, blastomycosis, and coccidiodomycosis are all known to be transmitted by the airborne route although sources of these fungi are usually found outdoors, and transmission from indoor sources is not common (Solomon and Burge 1984). *Aspergillus* species and, in fact, spores of any fungus capable of growing at body temperatures under conditions present in the respiratory mucosa can cause invasive disease in compromised hosts and are routinely present in air in most environments (Rhame et al. 1984; Solomon and Burge 1984). Fungi that can grow on skin (fungal dermatophytes) can be recovered from indoor air but have not been shown to cause disease via the airborne route (Solomon and Burge 1984). Protozoans that are known to colonize human hosts via the airborne route include *Pneumocystis carinii* (Hughes 1982) and *Acanthamoeba* (Mannis et al. 1986).

RESERVOIRS, AMPLIFIERS, DISSEMINATORS

For airborne disease transmission to occur in any environment there must be a source or reservoir for the microorganism, a means for the microorganism to multiply, particularly for a microorganism present in low numbers initially, and a mechanism for dissemination. A reservoir may serve as an amplifier and a disseminator, as in the case of many viral diseases, but reservoir, amplifier, and disseminator may be separate.

RESERVOIRS

Common reservoirs for organisms causing airborne infectious disease include man, other vertebrates, soil, water, and air. The principal reservoir of most airborne viral diseases is man (colds, influenza, measles, chickenpox) (Muchmore et al. 1981; Spendlove and Fannin 1983). Viral diseases of other vertebrates are rarely transmitted to man through the air (e.g., rabies). Man also provides the reservoir for the organisms causing many airborne bacterial diseases including tuberculosis and most nosocomial pneumonias and staphylococcal infections (Palmer 1984). Other vertebrates serve as reservoirs for diseases such as anthrax (Brachman, Kauffman, and Dalldorf 1966) and brucellosis. Since many bacteria that can cause infectious human disease are basically saprophytic, they can be maintained in inanimate reservoirs such as soil (*Clostridium*) or water (*Pseudomonas*, *Acinetobacter*) (Solomon and Burge 1984). *Legionella* can also be maintained in wet soil and water reservoirs if suitable associate organisms are present to provide necessary amino acids (Skaliy and McEachern 1979; Wang et al. 1979; Fliermans et al. 1981; Arnow et al. 1982). These reservoirs are often outdoors but can be a part of the indoor environment. For example, any stagnant water, whether indoors or out, can provide a reservoir for a variety of potentially infectious bacteria. Soil and birds serve as reservoirs for the primarily infectious fungi such as *Histoplasma* and *Cryptococcus* (Recht et al. 1982; Williams and Moser 1987). However, the major reservoir for fungi that cause opportunistic fungal infections is dead plant material in the outdoor environment. Spores of most fungi are present in outdoor air (the disseminator) whenever snow cover is absent and are consistently present in indoor air, as a result of penetration via air intake vents or other openings, or growth on wet interior surfaces following infiltration into the building (Solomon and Burge 1984). *Aspergillus*, as well as other fungi, frequently colonizes the nose, which provides a reservoir for this potentially dangerous pathogen (Kauffman, Burge, and Solomon 1988). Reservoirs for infectious protozoa are for the most part unknown but probably include water, soil, and possibly vertebrates (Mannis et al. 1986).

AMPLIFIERS

Amplifiers enable microorganisms to multiply to concentrations sufficiently high to ensure that airborne dilution and possible injury to the organism resulting from the airborne state do not prevent transmission. In many cases the reservoir and the amplifier are the same. For viruses, which must always have a living host to grow, reservoir and amplifier are always the same; similarly, for the bacterial diseases that are primarily transferred from human to human or other vertebrate to human host, reservoir and amplifier are also the same. In contrast, any disease transmissable by a unit dose (or very low number of organisms) can be transmitted directly from the reservoir without amplification. Such transmission occurs for some of the infectious fungal diseases (*Cryptococcosis*) and for most infectious diseases that occur in immunocompromised patients (Rhame et al. 1984). Bacteria (e.g., *Legionella* and *Pseudomonas*) and fungi can survive in an outdoor reservoir, penetrate indoors via potable water, makeup air, or other routes and then increase in numbers in an interior environment. *Legionella* is an excellent example; it can contaminate and grow actively in ventilation and plumbing system components if suitable moisture and temperature conditions exist and supporting microorganisms are present (Miller 1979; Fisher-Hoch et al. 1981). *Pseudomonas* and *Legionella*

frequently utilize appliances such as nebulizers and humidifiers as both reservoirs and amplifiers (Arnow et al. 1982). Fungi can grow on any surface on which adequate moisture and nutrients are present. Although most bacteria require an abundance of water, fungi are, in general, adapted for growth in relatively dry environments and can grow on apparently dry environmental surfaces (e.g., condensation on ventilation system surfaces, walls, and insulation or on scales of human skin in house dust) (Rhame et al. 1984; Solomon and Burge 1984). Requirements for amplification of protozoa are less well known. However, because protozoa are often recovered from the same environments utilized by the saprophytic bacteria, it is possible that the bacteria may serve as a food source for the protozoa (Solomon and Burge 1984). In contrast, virulent *Legionella* have been shown to infect protozoa and multiply intracellularly within food vacuoles (Fields et al. 1986).

DISSEMINATORS

Airborne transmission of infectious disease requires that the microorganism be introduced into breathing-space air in sufficient numbers for infection to occur. Although dissemination of organisms is always required to produce disease, the disseminator can be the same as the reservoir for diseases that require only a very small dose for infection (pneumonic plague, measles, chickenpox, and influenza). For example, human to human transfer of most viral and some bacterial diseases occurs through actions, often involuntary, of the human reservoir/amplifiers (e.g. sneezing, coughing, shedding of skin scales) (Letts and Doermer 1983; Spendlove and Fannin 1983). The measles virus has been shown to use both human and mechanical dissemination; the human produces the initial aerosol, but subsequent transmission to other locations takes place through mechanical ventilation systems (Riley 1982). Influenza viruses also may spread in this way. Organisms that can colonize components of building ventilation systems are growing in an environment with an inherent dissemination mechanism. Some mechanical devices, by their mode of operation, act as both amplifiers and disseminators. For example, *Legionella* grows in cooling towers, and the combined action of the water sprays and the air movement produces a droplet aerosol that contains infectious units (Miller 1979; Fisher-Hoch et al. 1981). Likewise, nebulizers and vaporizers, implicated as disseminators in other kinds of bacterial pneumonia as well as Legionnaire's disease, produce viable aerosols by their mode of operation (Arnow et al. 1982; Solomon and Burge 1984). Toilets, which are transitory reservoirs for a wide variety of human source microorganisms, can act as disseminators since aerosols are produced during flushing (Spendlove and Fannin 1983). Fortunately, few disease outbreaks, if any, have been traced to toilets. Showers, whirlpool baths, and jacuzzis have been implicated in outbreaks or single cases of infectious diseases such as legionellosis (Storch et al. 1979; Fraser 1985). All of these devices produce droplet aerosols during operation. The action of cleaning water reservoirs with vigorous mechanical agitation, such as high-power sprays, also can create a potentially dangerous aerosol if infectious microorganisms are present.

Organisms that survive and are infectious in a relatively dry state (e.g. fungus spores, bacterial spores) can be disseminated by even slight disturbance of their reservoir/amplifier. Vacuuming or walking on contaminated carpeting increases airborne levels of entrained viable particles (Rhame et al. 1984). Excavation of contaminated soil is a documented mode of dissemination for *Histoplasma*, *Blastomyces*, and *Cryptococcus*. Although initially suggested for *Legionella*, this mode is no longer considered plausible. Demolition of buildings also can produce infectious aerosols, which may be especially dangerous for immunocompromised hosts. Any aerosol, whether dry or droplet, that is produced outdoors near air intakes for ventilation systems or near open windows can enter the indoor air and cause disease among persons in the structure (Solomon and Burge 1984). Except for diseases with a very low dose requirement (e.g. cryptococcosis or any disease in a compromised host), outdoor exposure only rarely results in disease, probably because the large mass of outdoor air and its continuous movement tend to dilute aerosols rapidly.

FACTORS INFLUENCING AIRBORNE INFECTION

AEROSOL CHARACTERISTICS

In order to cause infectious disease through respiratory tract exposure, aerosols must be small enough to penetrate the respiratory tract (<5 μm) but large enough to contain the infectious agents in a viable state and in sufficient numbers to constitute an infectious dose (Knight 1973; Riley 1982; Willeke and Baron 1987). Most aerosols produced from water sources (human sneezing, coughing, water spray systems) are initially comprised of droplets too large to remain airborne, and those that do remain airborne are too large to penetrate the lower human respiratory airways. However, these large aerosols begin to desiccate immediately after generation because relative humidity in the range commonly found in most interiors is not high enough to maintain large droplet aerosols. Consequently, droplet nuclei are produced in a size range of particles that remain airborne for long periods of time and are small enough to reach the lower airways. After formation, such droplet nuclei are rapidly dispersed and become randomly distributed in the indoor air; if concentrations are sufficient, all susceptible persons inhaling the aerosol are at risk for disease. Fortunately, most droplets produced even from heavily contaminated sources carry relatively few viable agents, and dilution quickly lowers the potential dose below infective limits. If inadequate ventilation is present in an environment in which infectious aerosols are continually being produced and if the microorganism can survive aerosolization, very high rates of infection can result. For example, 72 percent of the passengers and crew of a commercial airliner that was on the ground for several hours without operating ventilation were infected with an influenza virus (Moser et al. 1979). For diseases such as measles or for highly susceptible compromised hosts for whom very small doses are effective, the risk of airborne transmission from droplet nuclei is high even in well-ventilated interiors.

THE DISEASE AGENT

Characteristics of disease agents that affect airborne transmission relate primarily to viability and virulence. Viability is influenced by the structure of the organism and its suitability for the environment. Organisms that produce spores or other resistant stages are most likely to remain viable in the aerosol state. Most fungi produce spores capable of survival during airborne travel. Desiccation, for example, has little effect on many fungal spores. In addition, many fungal spores contain melaninlike pigments that protect against damage from ultraviolet radiation. Some bacteria produce spores, bacterial endospores, that resist not only drying and ultraviolet radiation but survive at high temperatures and high atmospheric pressures and resist many biocides. Viral resistance to environmental stress appears to depend on the lipid content of the virus. In general, lipid-containing viruses tend to be more stable in air than lipid-free viruses (Loosli et al. 1943; Ijaz et al. 1985; Karim et al. 1985). However, both relative humidity and temperature have independent effects on survival of viruses, and the effects of these environmental factors differ widely for different viruses. Some of the slow viruses may be more resistant since they can survive autoclaving; however, their survival characteristics in air are unknown.

Survival of airborne bacteria is determined by equally complex interactions between structure and environment (Hambleton et al. 1983; Katz and Hammel 1987). One study indicated that *Legionella* survives best in aerosol at 65 percent relative humidity and is least stable at 55 percent relative humidity (Hambleton et al. 1983). Another study demonstrated a drop of viability by a factor of four logarithms during the first 30 seconds of aerosolization (Katz and Hammel 1987) and a similar drop of viability when growth substrate temperatures rose from 55 to 65°C. Survival of *Legionella* was also dependent upon whether the organism was in stationary or log growth phase when aerosolized. Stationary phase organisms survived at a higher rate.

The evidence indicates that infection rate varies with aerosol characteristics and viability and virulence of the organism, as well as the concentration of the virulent particles in the aerosol (Loosli et al. 1943; Arnow et al. 1982; Williams and Moser 1987). *Legionella*, for example, can be readily isolated from many sites within a hospital or an office building in which no illness has been documented. However, when amplification of *Legionella* of sufficient virulence occurs and susceptible people are exposed to the concentrated aerosols, illness results (Eickhoff 1979; Fraser 1985). A similar sequence of amplification and exposure has been demonstrated for influenza. In the influenza epidemic in an airplane, mentioned above, the virus apparently accumulated to an infectious level because of inadequate ventilation (Moser et al. 1979). The risk of such an epidemic occurring in a well-ventilated airplane, although not yet documented, is probably quite low (National Research Council 1986). On the other hand, some infectious agents can cause disease at very low concentrations. Riley (1982) has hypothesized that a single droplet nucleus containing the tuberculosis bacillus is potentially infectious. Also, as we have emphasized above, immunocompromised patients may be susceptible to serious infections from almost any agent, even when present in a unit dose. *Legionella* is no exception. Patients on corticosteroid therapy have been shown to be susceptible to legionnellosis from inhaled tap water aerosols that did not cause disease in matched patients not on immunocompromising therapy (Arnow et al. 1982).

In addition to environmental factors, virulence of most microorganisms is controlled by the genetic makeup of the organism. Strain to strain variability can occur. For example, for *Legionella*, only one of the several strains isolated from environments in which epidemics have occurred has been demonstrated to have caused infection (Fraser 1985). The effect of other indoor air pollutants on survival and virulence of microorganisms is unknown.

HOST FACTORS

Age, health, and immunity status (Centers for Disease Control 1984) are important factors in the host which determine susceptibility to infectious disease. In general, very young and very old people are at greater risk for most infectious diseases although middle-aged men appear to be at increased risk for Legionnaire's disease, possibly because of greater occupational exposure (Storch et al. 1979). Health status is by far the most powerful controlling factor in infectious disease rates. Any condition that impairs immunity or other host defenses will predispose to infectious disease (Arnow et al. 1982; Recht et al. 1982; Palmer 1984). These conditions include both intrinsic and acquired immunodeficiency syndromes, drug- or treatment-induced immunodeficiency (e.g., steroids, immunosuppressive drugs, chemotherapy, and radiation therapy), alcoholism, hematologic malignancy, and stress. Smoking, viral respiratory infections, stroke, drug overdose, and obstructive lung disease tend to impair lung defenses and increase the risk of bacterial pneumonias. Exposure to some common air pollutants may also increase the risk of infection (Melia et al. 1982). Nitrogen dioxide and ozone exposure have been shown to increase the rate of infection and decrease the survival time of mice exposed to pathogenic bacteria (Ehrlich 1980; Jakab 1987); on the other hand, sulfur dioxide does not have a similar effect in animal models of infection. The effects of nitrogen dioxide and ozone exposure on respiratory infections in humans have not yet been established and are under investigation. Mean daytime temperature appears to affect incidence of respiratory infection although the mechanism is not clear (Lidwell, Morgan, and Williams 1965). Relative humidity, although clearly affecting the disease agent, has not been documented to be related to host susceptibility to respiratory disease, in spite of widespread belief to the contrary (Anderson et al. 1974). In a study designed to test the effects of prolonged isolation on immunity to respiratory infection, a group of people who had spent six months in the Antarctic at relative humidities consistently below 25 percent showed no increased risk of infection from respiratory viruses in comparison with the general population of New Zealand, where relative humidities vary in the range common to most temperate environments (Jennings and Faoagali 1980).

Some human activities increase the risk of infection by increasing the chance of

exposure to a high dose of infectious aerosol. Workers who handle organic material are inevitably exposed to biologic aerosols. Fortunately, most such aerosols are not infectious for normal people and, at worst, cause a variety of hypersensitivity diseases. However, both brucellosis and anthrax can be transmitted to workers handling infected animal materials (LaForce et al. 1969; Solomon and Burge 1984). Laboratory workers are also at greater risk of contracting infections from disease agents handled in the course of their jobs. The most common laboratory-acquired viral diseases include infectious hepatitis, Venezuelan equine encephalitis, Newcastle disease, and Epstein-Barr virus. Laboratory-acquired infection with human immunodeficiency virus, type 3, is now documented. Bacterial diseases commonly acquired in laboratory exposure include brucellosis, typhoid fever, tularemia, and tuberculosis, many of which are aerosol-transmitted diseases.

PREVENTION OF AIRBORNE INFECTION

Airborne infection can be prevented if the organism can be removed from the environment or rendered nonviable or if susceptibility can be controlled by control of host risk factors or by immunization (Brachman, Kauffman, and Dalldorf 1966). Removal from the environment usually involves interruption of the reservoir/amplifier/disseminator sequence. If infection could result from human to human transfer, infectious individuals, both those functioning as reservoirs and those functioning as amplifiers and disseminators, can be isolated from the majority of susceptible persons. However, individuals with infectious diseases that are not considered life threatening cannot always be isolated, and in this case, dilution and filtration are the best solution. Increased ventilation has been shown to decrease rates of viral upper respiratory disease (Brundage et al. 1988). In a contaminated workplace, dilution of the air by clean-air ventilation or by removal of the organism by filtration must be done to prevent worker infection. In the case of the grounded airliner, provision of forced mechanical ventilation with no recirculation might have prevented the epidemic. In most indoor environments, ventilation rates as set out in the guidelines of the American Society of Heating, Refrigerating, and Air-Conditioning Engineers make airborne transmission of viral aerosols from human sources unlikely, providing the standards are met. However, recent efforts at energy conservation have tended to lower ventilation rates in many public buildings far below these standards, and many homes may not be adequately ventilated throughout the year.

Reduction of indoor saprophytic bioaerosols requires either preventing penetration of outdoor aerosols (either by filtration or by removing the indoor reservoir) or eliminating reservoirs and amplifiers in the indoor space. Most fungal aerosols that cause infectious disease in interiors enter from outdoors and can be kept out by adequate filtration. However, a few spores always penetrate even the best system, and prevention of amplification in the indoor environment is often necessary. The important controlling factor for indoor fungal growth is water, either as water vapor (relative humidity) or surface condensation or accumulation. In the range of 25–75 percent relative humidity, fungal spore levels are directly correlated with relative humidity. Above 75 percent relative humidity, conditions are apparently ideal for surface growth (Solomon and Burge 1984). Any standing water, especially with mineral scale or other solid substrates available, presents a suitable substrate for fungal growth. It should be noted that most fungal aerosols arising from indoor growth do not cause infectious disease except in compromised hosts. In such highly susceptible people, even very low concentrations of some fungi can present a high risk of life-threatening infection. Unfortunately, maintaining a perfectly clean environment for these people is rarely possible.

Stagnant water can also act as reservoir and amplifier for bacteria, including *Legionella*, and for protozoa. Standing water should not be permitted, especially in building ventilation systems. Cooling-coil drip pans should drain immediately, and humidification should be achieved by methods that do not allow the accumulation of microbial slimes. In general, biocides should not be added to water in ventilation systems because the biocide, like the organisms, can become aerosolized by operation of the ventilation system. When ventilation systems containing viable microorganisms are to be cleaned, the system should be turned off during cleaning, and all biocides should be removed prior to restarting. Airborne disease resulting from contaminated tap water usually results only in immunocompromised hosts (Stout, Yu, and Muraca 1987). Although disinfection of epidemiologically implicated potable water supplies as well as cooling towers is certainly necessary in epidemic situations (Soracco et al. 1983), routine disinfection (especially in nonhospital settings) to prevent disease transmission is questionable. Epidemics related to cooling towers involve direct exposure to the cooling tower aerosol (drift). Preventing exposure to this drift is a potential solution. Cooling towers should never be located in places in which the drift can enter air intakes or in which people can pass directly through the effluent; towers that are so placed should be maintained rigorously. It must be remembered that biocides added to cooling tower water will be released in the drift and may have adverse health effects.

SUMMARY

Airborne disease transmission involves a complex sequence of events involving a reservoir, amplifier, and disseminator. The mere presence of a pathogen in the environment does not necessarily lead to human illness. For infection to occur, the pathogen must be amplified and effectively disseminated to reach a susceptible host in a condition that is adequate to cause infection. Prevention of airborne infection can be effected by source, or reservoir, removal, or by interruption of the reservoir/amplifier/disseminator sequence.

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