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## Airborne Infectious Microorganisms<sup>☆</sup>

**Cristina Gonzalez-Martin**, University Institute of Tropical Diseases and Public Health of the Canary Islands, Canary Islands, Spain; University of La Laguna – ULL, Canary Islands, Spain

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### Glossary

**Aspergilloma** Pulmonary fungus ball consisting of a solid mass of hyphae growing in a lung cavity.

**Aspergillosis** Disease caused by the inhalation of some species of the genus *Aspergillus* resulting in growth of the fungus in the lungs.

**Bioaerosol** An airborne suspension of biological particles and microbial by-products.

**Blastomycosis** A symptomatic infection caused by the inhalation of the fungus *Blastomyces dermatitidis*.

**Chickenpox** Disease caused by the virus varicella-zoster.

**Coccidioidomycosis** Disease caused by the inhalation of *Coccidioides immitis* arthroconidia (also called San Joaquin Valley fever).

**Cryptococcosis** Disease caused by the fungus *Cryptococcus neoformans*.

**Endotoxin** A lipopolysaccharide component of the Gram-negative bacteria cell released during active cellular growth and after cell lysis that can cause respiratory distress when inhaled.

**Enteric viruses** Group of viruses related with the digestive system of hosts, including the genera Adenovirus, Calicivirus, Enterovirus, Rotavirus, etc.

**Fomite** An inanimate object that transmits infectious agents to a new host.

**H5N1, H7N2, H9N2, and H7N3** Strains of avian influenza A viruses that have been linked to respiratory disease in humans.

**Histoplasmosis** Disease caused by the infectious fungus *Histoplasma capsulatum* that can manifest as mild flu-like symptoms to chronic lung disease that resembles tuberculosis.

**HIV** Human immunodeficiency virus

**HPS** Hantavirus pulmonary syndrome.

**Legionnaires' disease** A severe respiratory disease resulting from the inhalation of *Legionella pneumophila*.

**Measles** Term for the disease caused by the virus of the same name.

**MERS** Middle east respiratory syndrome

***Mycobacterium tuberculosis*** The causative agent of human tuberculosis.

**NLVs** Norwalk-like viruses.

**Pontiac fever** A mild flu-like syndrome following inhalation of nonviable *L. pneumophila*.

**Rubeola** Another name for the disease measles.

**SARS** Severe acute respiratory syndrome.

**SARS-CoV** Severe acute respiratory syndrome associated coronavirus.

**Sin nombre virus** Causative agent of the majority of hantavirus pulmonary syndrome cases in the United States.

### Defining Statement

Inhalation of airborne pathogenic microorganisms can elicit adverse human health effects including infection, allergic reaction, inflammation, and respiratory disease. This article discusses viruses, bacteria, endotoxin, and fungi that are dispersed through the air and can result in infection following inhalation.

### Introduction

Inhalation exposes the upper and lower respiratory tracts of humans to a variety of airborne particles and vapors. Airborne transmission of pathogenic microorganisms to humans from the environment, animals, or other humans can result in disease. The lung is more susceptible to infection than the gastrointestinal tract as ingested microorganisms must pass through the acidic environment of the stomach before they can colonize tissue, while inhaled microorganisms are deposited directly on the moist

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surfaces of the respiratory tract. Inhalation of microbial aerosols can elicit adverse human health effects including infection, allergic reaction, inflammation, and respiratory disease.

## Bioaerosols

A bioaerosol is an airborne collection of biological material. Bioaerosols can be comprised of bacterial cells and cellular fragments, fungal spores and fungal hyphae, viruses, and by-products of microbial metabolism. Pollen grains and other biological material can also be airborne as a bioaerosol. Microbial aerosols are generated in outdoor and indoor environments as a result of a variety of natural and anthropogenic activities. Wind, rain and wave splash, spray irrigation, wastewater treatment activity, cooling towers and air handling water spray systems, and agricultural processes such as harvesting and tilling are examples of activities that generate bioaerosols outdoors. Indoors bioaerosols are generated and dispersed by mechanical and human activity. Industrial and manufacturing practices and biofermentation procedures can generate high concentrations of microbial aerosols. Heating, ventilation, and air conditioning (HVAC) systems, water spray devices (e.g., showerheads and humidifiers), and cleaning (e.g., dusting, sweeping, vacuuming, and mopping) result in the transport of microbial materials in the air. Talking and coughing generate bioaerosols from individuals, some of which may be infectious. Facilities with medical, dental, or animal care practices can generate infectious microbial aerosols.

The individual particle size of particulate material in bioaerosols is generally 0.3–100  $\mu\text{m}$  in diameter; larger particles tend to settle rapidly and are not readily transported in the air. Virus particles are nanometer in size, bacterial cells are approximately 1  $\mu\text{m}$  in diameter, and fungal spores are  $>1 \mu\text{m}$ . These microorganisms can be dispersed in the air as single units, but are often present as aggregate formations. The larger aggregates have different aerodynamic properties than single-cell units; therefore their dispersal may be different than single-unit particles. Aggregates of biological material also afford protection from environmental stresses such as desiccation, and exposure to ultraviolet radiation ozone and other pollutants in the atmosphere. Often bacterial cells and virus particles are associated with skin cells, dust, and other organic or inorganic material. During agricultural practices (e.g., during harvesting, and tilling), fungus spores are released from plant surfaces and the soil and raft on other particulate matter. This “rafting” affects the aerodynamic characteristics and the survival of the cells in the bioaerosol. When biological material is dispersed from water sources (e.g., splash, rainfall, or cooling towers and fountains), it is generally surrounded by a thin layer of water. This moisture layer also changes the aerodynamic properties and aids in the survivability of the microorganisms while airborne.

Airborne particulate will remain airborne until settling occurs or they are inhaled. Following inhalation, large airborne particles are lodged in the upper respiratory tract (i.e., nose and nasopharynx). Particles  $<6 \mu\text{m}$  in diameter are transported to the lung where the 1–2  $\mu\text{m}$  particles have the greatest retention in the alveoli. The average person inhales approximately  $10 \text{ m}^3$  of air per day, which may result in an infective dose for some airborne pathogens. Diseases resulting from inhalation of bioaerosols include allergic reaction, irritation, inflammation, infection, and respiratory disease.

The by-products of microbial metabolism and foreign proteins of microorganisms and fragments of cells can result in allergic reactions and irritant responses. The inflammatory response and allergic reactivity can be debilitating to sensitized individuals in indoor and outdoor environments, and it has been demonstrated following exposure to airborne bacterial fragments present in airborne dust. However, the greatest adverse health impact following exposure to airborne microorganisms is associated with inhalation of infectious agents. These infectious agents include viruses, bacteria, and fungi. The following sections introduce representative pathogens of each grouping that are associated with the airborne route of exposure. [Table 1](#) provides a summary of the pathogens presented in this article.

## Infectious Airborne Viruses

Viruses are noncellular units consisting of either DNA or RNA. They do not have self-directed biosynthesis and, therefore, require a living host cell for replication. Following inhalation, infectious viruses can establish in host cells of the respiratory tract. Some are translocated and infect the gastrointestinal tract and other tissues.

### Influenza

Influenza is a contagious respiratory illness caused by flu viruses A, B, and C. There are subtypes of influenza type A viruses based on two proteins on the surface proteins of the virus, hemagglutinin (H) and neuraminidase (N). Many animals carry influenza A viruses, while influenza B viruses circulate among humans. Both influenza types A and B viruses cause epidemics of disease almost every winter. Influenza type C infections cause a mild respiratory illness and are not thought to cause epidemics. While symptoms can be mild, influenza may result in severe illness and death. The Centers for Disease Control and Prevention reports that there are more than 200,000 hospital admissions and 36,000 deaths per year in the United States due to influenza. All ages can have serious illness from influenza, but those more likely to have complications are people aged 65 years and older, people with chronic medical conditions, and very young children. Transmission of influenza viruses is from person to person in respiratory droplets expelled during coughing and sneezing. The droplets are propelled usually less than 3 feet through the air and deposited on people in close proximity. The presence of the virus has been confirmed in aerosol particles within the breathable fraction in a study performed in a hospital emergency room ([Blachere et al., 2009](#)). Fomites contaminated with settled infectious droplets can also serve as a vehicle for transmission of influenza.

**Table 1** Characteristics of selected infectious microorganisms transmitted via the airborne route of exposure

Organism	Characteristics	Disease	Reservoir
<i>Aspergillus</i> spp.	Fungus, a mold with spherical spores ~1 µm in diameter, variety of species including <i>Aspergillus fumigatus</i> , <i>Aspergillus flavus</i> , <i>Aspergillus nidulans</i> , <i>Aspergillus terreus</i> , and <i>Aspergillus niger</i>	Aspergillosis, aspergilloma (fungus ball), allergic sinusitis, and allergic bronchopulmonary disease	Environment, compost and plant material, soil, dust, building materials
<i>Blastomyces dermatitidis</i>	Fungus; 8–15 µm spherical yeast cells	Flu-like illness, chronic lung disease	Moist soil enriched with decomposing organic debris
<i>Coccidioides immitis</i>	Fungus; 5 µm alternating barrel-shaped arthrospores	Coccidioidomycosis/ San Joaquin Valley fever	Desert soils with intermittent wet and hot dry cycles
<i>Cryptococcus neoformans</i>	Fungus; vegetative form (yeast cell) 2.5–10 µm, basidiospores 1.8–3 µm	Cryptococcosis	Pigeon droppings debris and soil associated with birds
Enteric viruses	Virus; RNA/DNA, ~20–100 nm	Gastrointestinal symptoms, meningitis, encephalitis, respiratory infections	Infected persons, surfaces
<i>Histoplasma capsulatum</i>	Fungus; dimorphic 2–5 µm oval cells	Flu-like symptoms, chronic lung disease, dissemination to other organ systems	Environment
Influenza viruses	Virus; single-stranded RNA, three distinct types (i.e., A, B, and C), 80–120 nm	Influenza, pneumonia, acute respiratory distress	Human respiratory secretions; avian flu associated with birds
<i>Legionella pneumophila</i> and <i>Legionella</i> spp.	Bacterium; vegetative Gram-negative bacillus, 0.5–1 µm by 2 µm	Legionnaires' disease and Pontiac fever	Ubiquitous in fresh and waste water environments, an intercellular parasite of protozoa
Measles virus (MeV)	Virus, enveloped, negative – sense, single-stranded RNA hantavirus, 100–250 nm	Rubeola: acute, febrile disease with an exanthematous rash, dry cough, sore throat, headache	Human – only known reservoir
Middle East respiratory syndrome – associated coronavirus (MERS-CoV)	Virus, enveloped, positive-sense single-stranded RNA	Acute respiratory distress syndrome, multi-organ failure, septic shock, death	Infected persons, bats and camels reservoirs
<i>Mycobacterium tuberculosis</i>	Bacterium; acid-fast, 0.2–0.6 µm by 1–10 µm	Tuberculosis	Infected persons
Severe acute respiratory syndrome – associated coronavirus (SARS-CoV)	Virus; RNA with helical symmetry, positive-sense single-stranded RNA	Acute respiratory distress	Infected persons
Sin nombre virus (SNV)	Virus; negative – sense, single-stranded RNA hantavirus	Hantavirus pulmonary syndrome (HPS)	Rodent urine, saliva, and feces especially <i>Peromyscus maniculatus</i> (deer mouse)
Varicella-zoster virus (VZV)	Virus; double-stranded DNA, 150–200 nm	Chickenpox	Humans – only known reservoir; virus may be dormant until reactivates as shingles

Avian influenza A viruses usually do not infect humans. However, cases of human infection with avian influenza viruses have been reported since 1997. Illness caused by several strains of avian influenza A viruses (e.g., H5N1, H7N2, H9N2, and H7N3) have been reported since 2004. The majority of human avian influenza infections have resulted from inhalation during direct contact with infected poultry or contaminated surfaces such as avian cages, or from the ingestion of uncooked blood of infected birds. Therefore, this influenza has been popularized as “bird flu.” The illnesses resulting from avian influenza infection in humans range from typical mild influenza-like symptoms (e.g., fever, sore throat, cough, and muscle aches) and conjunctivitis to more serious cases of pneumonia, acute respiratory distress, and other severe and life-threatening complications. To date, there have been no sustained human-to-human transmission of avian influenza A viruses, but because of the potential for these viruses to gain the ability to spread easily between people, monitoring for human infection and person-to-person transmission is important. In addition, recent studies have addressed the possibility of long-range transport of both, Influenza and Avian influenza viruses, using dust storms as a vehicle to be dispersed at farther distances (Chen et al., 2009, 2010).

### Severe Acute Respiratory Syndrome

Severe acute respiratory syndrome (SARS) is a newly reported respiratory illness. It was first reported in February 2003 in Asia. Since then, it has also been reported in North America and Europe. It is a viral respiratory illness caused by a coronavirus, termed SARS-associated coronavirus (SARS-CoV). Exposure to SARS-CoV results from close personal contact with infected individuals. Transmission is generally the result of touching the skin of an infected person or objects contaminated with infectious droplets and then

transferring the virus to the new host's eyes, nose, or mouth. Coughing or sneezing by an infected individual also releases droplets into the air that are propelled a short distance (<1 m) and deposited on the mucous membranes of the mouth, nose, or eyes of persons who are nearby. It is possible that SARS can be spread further through the air by very small particles, and although it may be unusual, it has been confirmed in different environments (housing complex, aircraft, hospital facilities) (Wong et al., 2004; Olsen et al., 2003; Yu et al., 2004). Hand hygiene, use of gown, gloves, and eye protection when in contact with an infected individual, and use of an appropriate respirator minimizes the spread of SARS.

### Middle East Respiratory Syndrome

Middle East respiratory syndrome coronavirus (MERS-CoV) emerged in 2012 in Saudi Arabia. Since then, a major outbreak occurred in 2015 in the Republic of Korea, and many other countries have reported positive cases (WHO, 2015). Human-to-human contact seem to be the principal way of transmission, however, its survival in aerosols has been positively tested, pointing to the airborne route as an alternative form of dispersal (van Doremalen et al., 2013). Genetic analyses of patients' specimens showed similarities between MERS-CoV and other coronavirus isolated from hedgehogs, bats and camels, suggesting their possible role as reservoirs (WHO MERS-CoV Research Group, 2013). Despite all these data, the exact way of transmission remains on debate. Pathology may vary from asymptomatic to have a fatal outcome. It starts with mild symptoms (fever, cough, etc.) followed by pneumonia with acute respiratory distress and multi-organ failure that may lead to death in 60% of the cases (WHO MERS-CoV Research Group, 2013; de Groot et al., 2013).

### Enteric Viruses

Enteric viruses primarily cause gastrointestinal infections, but may also be responsible for more serious diseases such as respiratory infections, meningitis or encephalitis (Fong and Lipp, 2005). Adenovirus, enterovirus, norovirus, hepatovirus and rotavirus are some of the genera considered within this group (Bosch, 1998). They are typically transmitted by fecal contaminated water or food, but airborne dispersion has been considered in some major outbreaks (Kuo et al., 2009; Marks et al., 2000, 2003; Xu et al., 2013; Dick et al., 1987; Ho et al., 1999; Lin et al., 2002). In the case of norovirus, which causes diarrhea and sudden projectile vomiting, it has been estimated that over 30 million virus particles can be liberated during vomiting. Since the infectious dose is very low,  $10^1$ – $10^2$  particles, airborne transmission within close contact is highly likely (Caul, 1994; Baert et al., 2008).

### Hantaviruses

Hantavirus pulmonary syndrome (HPS) is a life-threatening disease caused by rodent-borne hantaviruses. It is characterized by severe pulmonary illness and a mortality rate of 30–40%. The sin nombre virus (SNV) causes the majority of HPS cases in the United States, and *Peromyscus maniculatus* (the deer mouse) is its predominant reservoir. The virus found in the rodent urine, saliva, and feces becomes aerosolized as mist from urine and saliva or dust from feces. Inhalation is the most common route of infection. However, touching the mouth or nose after handling contaminated materials or being bitten by an infected rodent also result in infection. Hantavirus is not spread from person to person. Classic symptoms of disease include fever, fatigue, and muscle aches. Symptoms progress in 4–10 days to cough and shortness of breath.

### Measles

The disease measles, also known as rubeola, is contracted by inhalation of infectious droplets expelled as respiratory secretions by an infected individual. The only known reservoir of the measles virus (MeV) is humans. All strains of this virus belong to a single antigenic type and immunity is long lasting following infection.

Fever, malaise anorexia, and respiratory symptoms mimic other respiratory infections, but the appearance of Koplik's spots precedes a rash on the face that proceeds down the body to the soles and palms. Severe complications may occur including a chronic degenerative neurologic disease that occurs many years after a measles infection.

Measles is worldwide, but the success of vaccination programs in developed countries has limited the number of cases of childhood measles, decreasing the prevalence over 90% in Europe. However, there are still sporadic outbreaks, which cause more than 100,000 deaths, especially in patients from developing countries. An eradication program from the World Health Organization initiated in 2001 is promising if the appropriate measures are implemented (Holzmann et al., 2016). This program will not only have to assure the availability of the vaccines to developing countries, but also counteract the anti-vaccination movements that have increase the number of unvaccinated children in high-income countries in the recent years (Whelan, 2016; Dube et al., 2015; Kajetanowicz and Kajetanowicz, 2016).

### Varicella

Chickenpox is a highly contagious disease caused by the varicella-zoster virus (VZV). Chickenpox is usually a self-limited disease lasting 4–5 days with fever, malaise, and a generalized vesicular rash of blister-like lesions. The rash covers the body, but it is usually more concentrated on the face, scalp, and trunk. Serious complications including bacterial infections of skin lesions, pneumonia, cerebellar ataxia, and encephalitis may occur, but are rare. Disease is spread by aerosol dissemination of the virus during coughing

and sneezing by an infected person or it may become airborne directly from the skin lesions. Incidence of chickenpox is highest among children 1–6 years of age, but the licensing of a vaccine in 1995 and vaccination requirements for daycare and school children greatly reduced the impact of this virus in the United States in around 75% in a 10-year frame (2000–10) (WHO, 2014).

Following varicella infection, the virus becomes latent in sensory nerve ganglia and may reactivate later in life resulting in shingles. Airborne dispersion from herpes zoster patients may also occur and spread the virus to new varicella outbreaks (Saidel-Odes et al., 2010; Suzuki et al., 2004; Lopez et al., 2008).

## Infectious Airborne Bacteria

Unlike viruses that require a host cell, bacteria can colonize and grow on a variety of surfaces and in liquids when physical and nutritional factors are suitable. Therefore, bacteria can be released into the air from a variety of natural and anthropogenic environments. When infectious bacteria are released into the air, they can be readily transported via bioaerosols to susceptible individuals.

### Legionella

The first report of Legionnaires' disease followed the outbreak of respiratory illness among American Legion conventioners in Philadelphia in 1976. Currently an estimated 10,000–15,000 cases of Legionnaires' disease are reported in the United States per year. The causative agent, *Legionella pneumophila*, is a vegetative Gram-negative bacterium that is ubiquitous in freshwater environments worldwide. It survives as an intercellular parasite of protozoa thereby resulting in protection for the bacterium while in the environment. Infective aerosols can be transported up to 200 m from the source and can be generated from contaminated water spray devices such as showerheads, evaporative condensers, humidifiers and fountains, and also from cooling towers or waste treatment plants (Blatny et al., 2008, 2011).

Following the inhalation, *L. pneumophila* replicates in host macrophage resulting in severe pneumonia. While *L. pneumophila* accounts for the majority of disease cases caused by this genus, 19 other *Legionella* species are also human pathogens, often causing disease in immunosuppressed patients. *Legionella* bacteria that cannot replicate in the lung are cited as the cause of Pontiac fever, a mild flu-like syndrome. Often these organisms are released in aerosols from whirlpool tubs. Pontiac fever results in many more cases of illness, but fewer deaths; while Legionnaire's disease has a much higher mortality, but lower morbidity.

No human-to-human transmission has been documented. For an outbreak of Legionnaires' disease to occur, a series of events must happen. A reservoir of infectious bacteria must be present, the environmental conditions must be right for the concentration of organisms to increase, the organisms must be infectious and the infectious bacteria must be dispersed resulting in human exposure, organisms must be deposited in the appropriate site in the human host, and the host must be susceptible to infection by the *Legionella*.

### Other Gram-Negative Bacteria

*Escherichia coli*, *Pantoea* (*Enterobacter*) *agglomerans*, *Pseudomonas* spp., and *Acinetobacter* spp. commonly isolated in cow barns, pig houses, and poultry barns are among the airborne Gram-negative bacteria associated with animal facilities that can result in human disease. Special interest has been focused in the spread of antibiotic-resistance genes by these bacteria, not only among livestock, but also to humans. Alarming results have been observed and effective measures should be applied to stop their dispersal (Gandolfi et al., 2011; Gao et al., 2014; Li et al., 2016). Disease-causing Gram-negative bacteria are also dispersed into the air from wastewater treatment plants, vegetable and herb processing, recycling facilities and within hospital facilities.

These organisms can cause a variety of health problems, especially to the young, elderly, and immunocompromised persons.

### Endotoxin

Endotoxin is a lipopolysaccharide component of the Gram-negative bacteria cell and is released during active cellular growth and after cell lysis. While it is not an infectious particle and people are exposed to them daily, endotoxin is biologically active material derived from bacteria that can affect many human organ systems and disrupt humoral and cellular host mediation systems. Symptoms of exposure to airborne endotoxin include chest tightness, cough, shortness of breath, fever, and wheezing. Obstruction of airflow and exacerbation of asthma has been related to airborne endotoxin concentrations, and atopic and nonatopic asthma have been associated with endotoxin exposure because of its ability to induce inflammatory reactions. Repeated inhalation exposure has been shown to induce allergen-specific airway inflammation. The organic dust toxic syndrome (ODTS) is an acute inflammatory condition caused by high levels of endotoxin, usually resolves within 48 h, and has a prevalence of more than 20% among farmers. Severity of hypersensitivity pneumonitis (HP) can be increase under the influence of endotoxin exposure (Thorne and Duchaine, 2007).

Airborne endotoxin exposure is a concern in dusty occupational facilities such as cotton processing facilities and agricultural settings, and in industrial environments that utilize water spray components (e.g., machining fluids). Indoor airborne endotoxin is a

concern with humidified mechanical air conditioning systems. The presence of dogs, moisture, and settled dust increase the likelihood of airborne endotoxin in the home. Despite the evidences that high concentrations of endotoxin has over human health, no limits have been established to prevent it and no international standard protocol is available to obtain comparable results (Smets et al., 2016).

### **Mycobacterium Species**

*Mycobacterium tuberculosis* is recognized for its role as the causative agent of human tuberculosis. Infected individuals can spread pathogenic bacilli when coughing, talking, speaking, laughing, and sneezing. Aerial dissemination of pulmonary tuberculosis was confirmed back in 1959, and recent studies have shown the need for implementing prevention measures to avoid the spread of the disease and ultimately, eradicate it (Riley et al., 1959; Escombe et al., 2007; Fennelly, 2007).

Overcrowding and low-socioeconomic status are often contributing factors to the spread of tuberculosis as individuals are in close association and hygiene conditions are usually poor. The confined spaces of airplane cabins have been implicated in transmissions to passengers and flight crew members. Infectious aerosols resulting from the operation of suctioning instruments during medical treatment, manipulation of tuberculosis ulcers, drainage of necrotic tissue, and exposure during autopsy have also been cited as causes of nosocomial *M. tuberculosis* infections.

Also, nontuberculosis mycobacterial species can be transported via the air and result in disease. Respiratory infection in immunocompromised patients has been associated with members of the *Mycobacterium avium* complex. *Mycobacterium bovis* can also affect humans, especially in low-income countries, and airborne transmission has been suggested as a main form of dispersion (Gannon et al., 2007; Lan et al., 2016). *Mycobacterium leprae* bacilli have been reported from the nose blow of an untreated person with lepromatous Hansen's disease (leprosy), and *Mycobacterium terrae* isolated from a water-damaged building demonstrated inflammatory responses in mouse lung during laboratory experiments.

### **Gram-Positive Non-Spore-Forming Bacteria**

Numerous Gram-positive bacteria are usually disseminated from the skin, oral and nasal surfaces, and hair of humans. This group is more frequently isolated from air samples than Gram-negative bacteria, with *Staphylococcus* being the most common genus of non-endospore-forming Gram-positive bacteria isolated in indoor air samples (Okten and Asan, 2012; Gilbert et al., 2010; Yu et al., 2015). The presence of these cells in the air increases the likelihood of nosocomial infections in healthcare settings. Nosocomial infections by airborne pathogens and with antibiotic-resistant bacteria in hospital environments are transmitted among patients through aerosol dispersal from patients, staff, surfaces, and aspiration from respiratory instrumentation. Airborne dispersal of pathogens is also a concern in home care and assisted living environments.

Additionally, the Gram-positive actinomycetes have been associated with illness in occupants of water-damaged buildings. Often they are associated with fungi that colonize on surfaces and building materials following water intrusion. High concentrations of actinomycetes have been obtained in air samples from wastewater treatment plants, entailing an exposure risk, not only for workers, but for the nearby population (Awad and El Gendy, 2014; Li et al., 2012).

### **Infectious Airborne Fungi**

Fungi are ubiquitous in nature. They utilize organic matter for their metabolism. Depending on the genus, they can readily disperse spores, cellular fragments, or cells into the air. Infectious fungi can cause serious mycoses of the respiratory tract and some are disseminated to the bone and other systems in the body.

#### **Histoplasma capsulatum**

Inhalation of spores of the fungus *H. capsulatum* can result in histoplasmosis. This disease is not transmitted from an infected person or animal to someone else but is the result of airborne transport from environmental surfaces and it is the most frequent mycosis in the United States (Cano and Hajjeh, 2001). Histoplasmosis primarily affects a person's lungs, and its symptoms vary greatly. Infected people are generally asymptomatic or they experience mild flu-like symptoms not requiring medical attention. Chronic lung disease resulting from infection with *H. capsulatum* resembles tuberculosis, and can worsen over months or years. The most severe and rarest form of histoplasmosis occurs when it is disseminated involving spreading outside the lungs. If untreated, disseminated histoplasmosis is fatal and has emerged as an opportunistic pathogen in HIV (human immunodeficiency virus) positive people (Cano and Hajjeh, 2001).

*H. capsulatum* is a dimorphic fungus with a mold (mycelial phase) when it is growing in soil at ambient temperatures, and a yeast phase after being inhaled by humans or animals. It has a global distribution in temperate zones, usually closely to rivers (Baumgardner, 2012; Chakrabarti and Slavin, 2011). The mold spores are either microconidia ranging from 2 to 5  $\mu\text{m}$  in diameter or macroconidia ranging from 8 to 15  $\mu\text{m}$ . The yeast cells of *H. capsulatum* are oval to round in shape with diameters ranging from 1 to 5  $\mu\text{m}$ .

### Coccidioides immitis

Inhalation of airborne *C. immitis* arthroconidia may result in the disease coccidioidomycosis (also called San Joaquin Valley fever). A cryptic species, *Coccidioides posadasii*, presents a different distribution and characteristics, but it can also cause coccidiomycosis and its dispersion through the airway route (Welsh et al., 2012). Within 48–72 h after inhalation and deposition in the lung, the arthroconidia change into spherules and develop numerous endospores. When spherules rupture, they release endospores which have the capacity to develop into a mature spherule.

Approximately 40% of those who become infected are symptomatic with flu-like illness with fever, cough, headaches, rash, and myalgia. Some individuals fail to recover and suffer chronic pulmonary infection. It accounts for 29% of pneumonia cases in endemic areas (Baumgardner, 2012). Around 5% will develop widespread disseminated infection that may affect the soft tissues, joints and bone, or meninges (Welsh et al., 2012). Coccidioidomycosis meningitis may lead to permanent neurologic damage. The immunocompromised and HIV-infected persons suffer severe pulmonary conditions and diffuse lung disease.

*C. immitis* grows in the soil of semiarid areas. It is primarily found in the Lower Sonoran life zone and is endemic in the southwestern United States; it is also found in parts of Mexico and South America. Exposure to airborne arthrospores occurs after disturbance of contaminated soil by humans or natural disasters (e.g., dust storms and earthquakes). Association with dust storms has been well documented, with significant outbreaks following a dust storm, with a marked seasonality during the drier and dustier months of the year (Griffin, 2007; Goudie, 2014). Persons in areas with endemic disease who have occupations exposing them to dust (e.g., construction or agricultural workers, and archeologists) are at risk. African-Americans and Asians, pregnant women during the third trimester, and immunocompromised persons have a higher risk than others.

### Blastomyces dermatitidis

Blastomycosis is an infection caused by the dimorphic fungus *B. dermatitidis*. This fungus grows in moist soil that is enriched with decomposing organic debris, and it is endemic in parts of the southcentral, southeastern, and mid-western United States. It is also present in some areas of Central and South America and parts of Africa and India. Exposure is via the inhalation of airborne spores, generally after disturbance of contaminated soil. Generally, individuals who frequent wooded areas with endemic disease (e.g., farmers, forestry workers, hunters, and campers) are the most exposed ones.

There are <1 to 100 per 100,000 population in areas with endemic disease. The infection may be asymptomatic or result in a flu-like illness with fever, chills, productive cough, myalgia, arthralgia, and pleuritic chest pain (Baumgardner, 2012). However, some infected individuals fail to recover and develop chronic pulmonary infection and permanent lung damage. Other individuals develop widespread disseminated infection that may involve the skin, bones, and genitourinary tract, and occasionally the meninges of the brain are affected. The mortality rate for blastomycosis is approximately 5%.

### Cryptococcus neoformans

*C. neoformans* var. *neoformans* causes most cryptococcal infections in humans. Infection with this yeast-like fungus can cause disease in apparently immunocompetent and immunocompromised persons, but most people do not get sick with cryptococcosis. Patients with T-cell deficiencies are the most susceptible to infection, and in the United States 85% of cases occur in HIV-infected persons. While the initial pulmonary infection is usually asymptomatic, cryptococcosis can cause serious symptoms of brain and spinal cord disease, such as headaches, dizziness, sleepiness, and confusion. Disseminated infection, especially meningoencephalitis, occurs in most patients.

*C. neoformans* var. *neoformans* is found worldwide, and its habitat includes debris around pigeon roosts and soil contaminated with decaying pigeon or chicken droppings. Exposure generally occurs when dried bird droppings are disturbed and dust containing *Cryptococcus* disperses in the air. The exact nature of the infectious particles of *C. neoformans* is not known, but they are likely to be dehydrated yeast cells or basidiospores of the appropriate size range to be deposited in the lungs. Once in the lung, the yeast cells become rehydrated and acquire the characteristic polysaccharide capsule. Virulence of this organism is associated with the ability to produce the large capsule and shed great amounts of capsular material into the body fluids of the host.

### Aspergillus

Aspergillosis is an invasive pulmonary infection with fever, cough, and chest pain. A localized pulmonary infection occurs for immunocompetent persons who have an underlying lung disease. The fungus infection may disseminate to other organs, including brain, skin, and bone. Exposure may also result in allergic sinusitis and allergic bronchopulmonary disease. A variety of *Aspergillus* species have been implicated.

*Aspergillus fumigatus* and *Aspergillus flavus* most often have been cited, but *Aspergillus terreus*, *Aspergillus nidulans*, and *Aspergillus niger* have also been associated with the disease. These fungi are ubiquitous in the environment, and their conidia (spores) are disseminated from soil, compost piles and other decomposing plant matter, household dust, building materials, and ornamental plants. Among with other genera (*Cladosporium*, *Penicillium* or *Alternaria*), *Aspergillus* is one of the most frequent fungi isolated from air samples, both in indoor and outdoor environments (Mahieu et al., 2000; Cao et al., 2014; Hwang et al., 2016; Oberle et al., 2015; Oh et al., 2014; Grishkan et al., 2012). Water-damaged buildings can also be a source for exposure, and infections have been



associated with dust exposure during building renovation or construction. To decrease workers and nearby population exposure to high levels of *Aspergillus* spores, certain construction works can be restricted to cooler seasons, which seem to influence the growth of the fungus (Pilmis et al., 2016).

## Airborne Bioterrorism

The threat of purposeful transmission of airborne pathogenic microorganisms and microbial toxins as weapons of mass destruction (WMD) has increased the awareness of the importance of bioaerosols. The Centers for Disease Control and Prevention and the Department of Health and Human Services have listed several pathogenic microorganisms as select agents. Of these, *Francisella tularensis*, *Yersinia pestis*, *Bacillus anthracis*, and *Variola virus*, the causative agents of tularemia, plague, anthrax, and smallpox, respectively, are ones that can be dispersed via aerosol and, therefore, are a concern for inhalation infection. Moreover, availability of new technologies, such as genetic engineering, may provide the tools to modify innocuous microorganisms or the transmission routes of other pathogens, involving a higher biosafety risk for the population (MacIntyre, 2015). Continued researches and awareness by public health professionals are needed to recognize these diseases and minimize the risk of exposure of the population. For example, the uses of biosensors to detect airborne pathogens are being developed and installed in official buildings and strategic sites, that allow a rapid detection and intervention (Fronczek and Yoon, 2015).

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