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Literature Review of the Effect of Temperature and Humidity on Viruses

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ABSTRACT

An extensive literature review of more than 120 papers was conducted on the effect of humidity and temperature on the transmission of infectious viruses. This review targets infectious viruses known to be transmitted through the air as well as direct and indirect contact. Evidence is cited from both direct and indirect study results examining environmental conditions that affect infectious disease aerosol transmission in enclosed environments. These results will have a major influence on the choice of infection control measures in indoor environments as well as an associated cost for equipment and renovations to the ventilation system or room design.

OVERVIEW

We examined each paper's data and assumptions in its totality rather than reviewing just the abstract and conclusion. We found that each study and methodology had certain limitations, and it is nearly impossible to compare one study to another because definitions and design parameters differ from study to study. It is important to understand the general design of infectious viral transmission studies and the role that viral composition and aerosol particle dynamics play in order to put the effect of temperature and humidity on viral transmission in context. There have been very few controlled human to human viral transmission studies. Since no animal model used to date (mice, ferrets, squirrel monkeys, and others) accurately displays human symptoms, the results of the animal studies are difficult to extrapolate to natural transmission of viral disease to and between humans via the exhalation and surface contact routes (Lowen et al. 2006, 2007a, 2007b, 2008, 2009; Andrewes and Glover 1941; Maines et al. 2009; Wells and Brown 1936; Frankova 1975; Ehrlich and Miller 1971; Elazhary and Derbyshire 1979). Results from observational and epidemiologic human studies are equally difficult to interpret due to the many confounding factors inherent in the study design including the lack of controls, inability to identify an index case, and incomplete or unavailable data. It also has been noted that data from uncontrolled observational studies have the potential for observation bias, confounding, co-intervention, or chance variation (Brankston et al. 2007). Hermann (2007) states, "Inconsistent replication of airborne transmission under experimental conditions suggests that we do not understand the conditions required for its occurrence." There is evidence in the literature as far back as 1943 (Loosli et al.), that the amount of virus inhaled is not easily quantified nor has anyone closely examined the specific mucosal lining conditions (i.e., duration of exposure) necessary for viral infectivity to occur. Airborne viruses may also have indirect effects such as triggering immune mediated illness, e.g., asthma (Arundel et al. 1986; Hersoug 2005).

Blachere (2009), using reverse transcriptase-polymerase chain reaction (RT-PCR) to detect naturally produced influenza bioaerosols of influenza viruses in a hospital setting, noted that detection by RT–PCR alone does not necessarily imply infectivity. For example, other factors such as host response, receipt of vaccine against the strain of influenza in circulation, use of respiratory hygiene practices, and avoiding crowded environments by the individual with acute infection all influence any one person's risk of infection following exposure. The literature suggests that different symptoms appear to have different duration of time below which the effects of low humidity are not noticeable (Nagda and Hodgson 2001). Any or all of these factors make definitive interpretation of the data questionable.

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Most of the available evidence for airborne transmission is based on poorly controlled viability studies related to the effects of artificially aerosolized viral particles on animal susceptibility. Many studies have shown that influenza viruses can survive in an artificially generated airborne aerosol for varying amounts of time and at varying temperature and humidity ranges and that these experimental aerosols may cause infection in both human beings and animals (Hemmes et al. 1960; Harper 1961; Schaffer et al. 1976; Ijaz et al. 1985; 1987. Karim et al. 1985; Ehrlich and Miller 1971; Lowen 2007a, 2007b, 2008, 2009). However, Brankston et al. (2007) note, "we question whether these studies are relevant to the natural route of human transmission. The artificial aerosols studied were quite different from natural aerosols generated by coughing."

Most studies do not account for the duration of time spent in the space in relation to the environmental conditions. Thus it is important to realize that to date, there is no conclusive evidence suggesting a defined minimum or maximum relative humidity (RH) that reduces viral survival to the point where a virus is less able to survive or is affected in its ability to cause an infection.

RH describes the amount of water vapor held in the air at a specific temperature at any time, relative to the maximum amount of water vapor that air at that temperature could possibly hold. At higher temperatures, air can hold more water vapor and the relationship is roughly exponential, i.e., air at higher temperatures can hold much more water vapor than air at lower temperatures.

Viruses—General

A virus is a small infectious agent that can only replicate inside the living cells of organisms. Virus particles consist of either DNA or RNA, a protein coat that protects these genes, and in some cases an envelope of lipids that surrounds the protein coat when they are outside a cell. Viruses vary in shape from helixes to much more complex structures.

Viruses do not all behave alike so there is unlikely to be a single explanation for a mode of transmission that can be extrapolated to include all viruses collectively, all viruses of a single strain, or how a particular strain affects a particular species.

For information on healthcare associated infections, please see the appendix.

Emerging Influenza Strains of Significance

Some of the most recently identified viral strains are H1N1, H5N1, SARS-CoV, and influenza A and each has its own unique characteristics (WHO 2006, 2008). Coronaviruses (CoV) in humans are responsible for causing many respiratory tract infections and have been linked to gastroenteritis (Lai and Holmes 2001; Holmes 2001). It is surmised that SARS-CoV is a mutated form of a coronavirus found in an animal that has contact with humans (Sharma and Khuller 2001). SARS was first identified in Guangdong Province in Southern China (Guan et al. 2003). It raised concerns because of its severity and seeming ease of transmission. Yet it has been shown that SARS can be brought under control using simple, well known health measures. The influenza A pandemic (H1N1) flu has two genes from flu viruses that normally circulate in pigs in Europe and Asia plus avian genes and human genes (Rambaut et al. 2008).

Since the 2009 emergence of H1N1 virus in people in Mexico as reported by Dawood et al. (2009) and Ginocchio et al. (2009), H1N1 flu has spread to 156 countries with at least 140,000 cases confirmed and 850 deaths. However, it has not been well researched.

H5N1 flu virus is an influenza A virus subtype that is a highly contagious and deadly variety among birds. Avian influenza strains are generally transmitted between birds via the fecal–oral route, yet transmission of avian strains to human beings is believed to occur mostly via direct contact between infected bird secretions and human respiratory mucosa (CDC 2005). The H5N1 flu virus does not usually infect people. Nearly all human cases have resulted from people having direct or close contact with H5N1-infected poultry or H5N1 contaminated surfaces. There have been very few cases of human-to-human transmission. Flu recipients in such cases have all died and there was no further spread (Class et al. 1998).

Temperature and Humidity

The ranges for low, medium, and high RH and temperature as referred to in the literature vary and do not have scientifically determined demarcations. Also, the literature shows opposing conditions for transmission of viruses ranging from low RH and high RH with temperature a secondary factor (Knight 1980; Harper 1961; Hemmes et al. 1960) making it difficult to interpret the full complement of results. Some experts believe that temperature is one of the most important factors affecting virus survival, as it can affect the state of viral proteins and the virus RNA or DNA. Viruses containing DNA tend to be more stable than RNA viruses. Generally, as temperature rises, virus survival decreases. Maintaining temperatures above 60°C (140°F) for more than 60 min. will usually inactivate most viruses, though this can vary depending on the presence of organic material (e.g. blood, feces, mucus, saliva, etc.) that may surround exhaled viral particles and insulate the virus against extreme environmental changes. Higher temperatures for shorter times can be just as effective to inactivate viruses (Tang 2009).

Modes of Influenza Transmission

The mode of influenza transmission and particularly the role that airborne transmission plays in the spread of influenza and other viral diseases has been studied and debated for over 70 years. There are four basic modes of infectious disease transmission: direct contact, indirect contact, droplet transmission, and airborne transmission. Contact transmission includes direct contact, indirect contact, and large droplet transmission.

Droplet and contact transmission require close contact to occur. It is well established that influenza is transmitted primarily through close contact, such as during exposure to large respiratory droplets, direct contact, short-range exposure to infectious aerosols, or perhaps a combination of these routes. However, the relative contribution and clinical importance of each of these modes of transmission has not been established.

Other factors may have an indirect effect on infectivity and degree of illness. Studies have shown that there is an inverse correlation between serum 25-hydroxyvitamin D (25-h D) levels and upper respiratory tract infection (URTI) (Cannell et al. 2006, 2008, 2009).

Vitamin A may be a significant factor since vitamin A shows a strong influence on measles (Coutsoudis et al. 1991), which is an enveloped virus spread by aerosol. There is some evidence for an effect on viruses by exposure to ozone (Hanley and Borup 2010). It is generally accepted that ultraviolet (UV) light is harmful to both viruses and bacteria under certain conditions (Myatt et al. 2003; Walker and Ko 2007), yet two studies with *S. marcescens* showed an increased survival in the presence of UV light at higher RH levels. This may be due to the protective effect of larger particle sizes, as evaporation would be less at these higher RH levels, thus indicating a protective effect of a thicker water coat against UV radiation (Riley and Kaufman 1972; Ko et al. 2000). All of these factors need continued study in order to include them properly in our understanding and epidemiological models.

Airborne Transmission

There is essential agreement that not every exposure to an infectious virus leads to infection or that virulence of a particular strain causes the same intensity of illness in all individuals (Burge and Feeley 1991). The incidence of illness and infectivity of a virus that is transmitted by the airborne route in an indoor environment is the result of a host of factors. These include humidity, temperature, population density, number of susceptibles, length of exposure, number of infected people producing contaminated aerosols, ventilation rate, infectious particle settling rate, whether the virus has a lipid or non-lipid envelope, the presence of surrounding organic material, exposure to Ultraviolet (UV) light or antiviral chemicals, microorganism resistance to antibiotic or antiviral therapy, type and degree of invasive procedures, spatial considerations such as seating or sleeping arrangements and contact with a carrier, persistence of pathogens within hosts, immuno-epidemiology, evolution and spread of resistance and role of host genetic factors.

Surfaces

Another source of viral transmission has been documented to occur from porous and non-porous surfaces to the hands of volunteers in large enough quantities to potentially cause disease. Although temperature and RH may affect virus survival on surfaces, infection resulting from contact with contaminated objects in the environment was not investigated. Bean et al. (1982) and Boone and Gerba (2005) showed that human influenza viruses could survive on a variety of surfaces at 35%–49% RH and a temperature of 28°C (82.4°F). Both influenza A and B viruses were cultured from experimentally contaminated, nonporous surfaces, such as steel and plastic, up to 24–48 h after inoculation and from cloth, paper, and tissues up to 8–12 h after inoculation. However, viruses could be recovered from hands for only 5 min and only if the hands were contaminated with a high viral titer. Viable virus could be transferred from nonporous surfaces to hands for 24 h and from tissues to hands for 15 min. These data support the feasibility of the spread of influenza by indirect contact. However, the importance of this mode of transmission probably depends on the type of surface and the amount of virus present. The SARS virus may survive on surfaces for days at temperature and humidity levels common to indoor environments. The role that environmental factors, such as air temperature and RH play in surface survival is important for risk assessment and the development of control measures.

Human Reservoirs

Viral diagnosis samples suggest the possibility that some other virus infection may have interfered with the spread of the influenza pandemic. Linde et al. (2009) reported that when H1N1 virus began to appear less frequently there was a prevalence of rhinovirus in about a third of the samples. Rhinovirus epidemics occur soon after school has started. The virus is spread mainly by contaminated hands, and has not been reported to be climate-dependent. A possible explanation for the sudden interruption of the spread of influenza could be the increase in the spread of rhinoviruses which may have a selective advantage over influenza due to the mild and moist climate. Although the laboratory data supporting this hypothesis are limited, it may stimulate research into the possibility that the interaction between different circulating viruses may affect influenza epidemiology.

The use of surrogates for modeling viral exposure, the risk of transmission, and control measures for pathogenic enveloped viruses, such as SARS-CoV and influenza virus may improve the examination of viral transmission on health care surfaces (Casanova et al. 2010).

Aerosol Particle Dynamics

When reviewing the literature, it is important to verify the size of the particles being studied and the authors' definitions of those sizes. It is also important to take into account the conditions under which the study is conducted and whether the particle transmission is induced mechanically or naturally.

The main sources of infectious airborne pathogens in enclosed environments are respiratory droplets generated when an infected person breathes, coughs, sneezes, or talks. An exhaustive search of the literature indicates that there have been very few studies on how exhalation flows interact with the room ventilation system. A recent systematic review conducted by Li et al. (2007) demonstrated that an inefficient

ventilation system causes the spread of airborne disease, whereas an efficient ventilation system can help mitigate the spread of infectious particles and thereby reduce transmission of disease. Room air flow is governed by a combination of air movements caused by ventilation, differences in temperature and moving bodies and equipment. These complex air movements make the route and suspension time of an infectious particle very difficult to determine once it has left the infectious host. There is essential agreement that particles with an aerodynamic diameter of 5 μm or less are aerosols, whereas particles of 20 μm are large droplets. Pathogen-laden droplets expelled into the air by an infected person subsequently dry out in the room air environment and produce fine particles and droplet nuclei that are suspended in the air currents. Aided by the ventilation system, the droplets may spread over a wide area. Although the liquid evaporates, the residual droplet nuclei may remain in the air for long periods of time depending on factors such as particle size, velocity, density, force of expulsion, particle density, humidity and rate of air flow. The disease-causing organisms then are inhaled by or come to rest on or near a susceptible person who may become subsequently infected. Clinical symptoms and outcomes in animals and people are different when exposed to aerosolized virus versus intranasal inoculation. Consideration must be given to differing quantities of intranasal inoculums and particle size as well (Couch et al. 1966; Mumford et al.1990; Loosli et al. 1943; Klontz et al. 1989; Morens and Rash 1995). Again, as Burge and Feeley (1991) point out, not every exposure to an infectious virus leads to infection nor does the virulence of a particular strain cause the same intensity of illness in all individuals.

Clinically applicable distinctions are made between short-range airborne infection routes between individuals, generally less than 1 m apart (3.28 ft) and long-range routes generally greater than 1 m (3.28 ft) distances. The literature describes smallpox studies in which droplets from patients could reach persons located 1.83 m (6.0 ft) or more from their source (Downie et al.1965; Wong et al. 2004). Small droplets may participate in short-range transmission, but they are more likely than larger droplets to evaporate to become droplet nuclei and then be considered as having the potential for long-range airborne transmission. True long-range aerosol transmission becomes possible when the droplets of infectious material are sufficiently small to remain almost indefinitely airborne and to be transmitted over long distances. Larger droplets with more mass are more strongly influenced by gravity and less so by air flows, and move more "ballistically," falling to the ground more quickly. Smaller droplets with less mass are less influenced by gravity and can be transported as a cloud over greater distances by air flows.

Respiratory droplets carrying infectious pathogens transmit infection when they travel directly from the respiratory tract of the infectious individual to susceptible mucosal surfaces of the recipient (Lillehoj and Kim 2002), generally over short distances. The distance droplets travel depends on the velocity and mechanism by which respiratory droplets are propelled from the source, the density of respiratory secretions, environmental factors such as temperature and humidity, and the ability of the pathogen to maintain infectivity over that distance. Particle movement in air is determined by Stokes' settling law which governs how quickly a sphere falls under the opposing forces of gravity downwards and air friction upwards (Evans and Jaegar 1975).

Cole and Cook (1998) and Wells (1955) report that sneezing can introduce as many as 40,000 droplets which can evaporate to produce droplets of 0.5 to 12 μm. Fitzgerald and Haas (2005) report that a cough can generate about 3000 droplet nuclei, the same number as talking for 5 minutes. A single cough typically produces about 1% of this amount, but coughs occur about ten times more frequently than sneezes (Duguid 1945). Since droplet transmission is a form of contact transmission, some infectious agents transmitted by the droplet route also may be transmitted by the direct and indirect contact routes. Normal breathing actually generates more bio-aerosols than a cough or a sneeze. The particles making up aerosol in normal exhalation are less than 1 micron in size and these smallest particles are primary vectors of contagion (Knight 1980; Tang et al. 2006; Papineni and Rosenthal 1997). The evidence suggests that very few respiratory viruses are exclusively transmitted via one route. There is no exact particle size cut-off at which pathogen transmission changes from exclusively droplet to airborne or vice versa. Rather, as particle sizes decrease below 5 μm, droplet transmission presumably blends into airborne transmission (Knight 1980). Preventing droplet and contact transmission would require very different control measures.

The mechanisms by which microorganisms infect tissue and produce disease are complex and incompletely understood. Some pathogens may contain or produce toxins or other substances that increase their ability to invade a patient's tissue, produce damage or survive in the tissue. Hanley and Borup (2010) note that depending on the composition and shape of the virus, different viruses may react to osmotic pressure in different ways, making some more virulent than others in the respiratory tract.

Influenza virus infects the columnar epithelium lining the respiratory tract and can cause infection in both the upper and lower airways with a typical average incubation period of two days (Morris et al. 1966). Foy et al. (1981) reports that although approximately 50% of influenza infections may be asymptomatic, infected persons with few or no signs of illness may still shed virus and may be infectious to others. Infected persons can become contagious the day before symptoms begin and can shed virus for an average of four days as discussed in Morris et al. (1966) and Murphy et al. (1973).

CASE STUDIES

An example of the possible affect of numerous confounding transmission factors can be found in a frequently cited aircraft study by Moser and colleagues (1979) describing an influenza outbreak that occurred on an Alaskan Airlines flight.

During a stop-over, the ventilation on the plane was shut down for 3 h during which time passengers became restless and moved about the cabin. One passenger on the flight, the supposed index case, became acutely ill with laboratory confirmed influenza A and 72% of the other passengers confined to the aircraft subsequently became infected with influenza. The occurrence of infection increased with increased time spent on the aircraft. There was no clear evidence for a single mode of transmission and at first glance this suggests transmission via the airborne route. However, there are several confounding variables that pointed to droplet or contact transmission from the index case. These included free movement of passengers throughout the aircraft cabin resulting in probable touching of surfaces that contaminated their hands; the index was seated near the restroom so almost all passengers passed by the index case during the layover, and the aircraft HVAC was inoperable. Thus, the passengers who became ill may have been infected by any of the common modes of transmission. Neither temperature nor humidity was considered in this study. A more recent "natural experiment" involved pH1N1 among members of a tour group to China. Despite several hours in flight, there were almost no cases of secondary transmission on the flights. This same group spent several hours on a commercial tour bus and the only secondary cases were reported among those who sat directly in front of or behind the index case or ate lunch with this initially infected person.

Klontz et al. (1989) reported a military aircraft outbreak study involving two planes with fully functioning ventilation systems that had 15 air changes per hour (ACH) in the passenger cabin and directional airflow from the ceiling to floor with minimum horizontal airflow. Within 72 h of deplaning, 56% of the people from both planes became ill. There was a significant difference in risk of acquiring influenza observed between the two aircraft that appeared to be related to the number of symptomatic persons on board. The epidemiologic data shows that secondary transmission of influenza to family members and roommates occurred in the days following the initial cases. Movement on the plane was not mentioned as a possible factor in transmission. It is difficult to draw conclusions regarding the mode of transmission in this study due to the lack of controlled scientific evidence to support any single or combined factor(s).

A study by Drinka et al. (2000) of a long term care facility reported an association between influenza infection and ventilation system design in different buildings. The higher the percent of outside air circulated in the buildings generally the lower the percent of patients infected.

The CDC published a study by Han et al. (2009) which has significant import in the study of airborne transmission of viral disease. An outbreak of influenza A pandemic (H1N1) occurred in June 2009 among members of a tour group in China who had traveled in the same tour bus for 7 h. Apparently, the index case-patient noticed flu like symptoms prior to arriving in China. Secondary cases developed in 30% of the tour group members who had talked with the index patient and in one other passenger who had sat within two rows of the index case-patient. Tour group members who had not talked with the index patient did not become ill. In conclusion, this 2009 outbreak of H1N1 pandemic virus infection was caused by transmission during coughing or vocalization by an imported case-patient. The virus spread by droplet transmission when the index case-patient was talking with fellow tourists. The findings of this investigation highlight the importance of preventing droplet transmission during a pandemic.

EFFECT OF ENVIRONMENTAL FACTORS ON VIRAL TRANSMISSION

Climate

Despite the fact that virulent strains of influenza virus are currently the major global concern for causing pandemics, the literature shows that there have been relatively few incidence-climate studies performed on influenza.

Numerous researchers described investigations of the possible associations between climate and respiratory viruses such as respiratory syncytial virus (RSV) which causes mild, cold-like symptoms in adults and older healthy children, SARS, and influenza (Thompson et al. 2003; Thompson et al. 2006; Tang 2009). There is some evidence that latitude may play a role in viral transmission and seasonality as there is such great variability in the study results (Vibaud et al. 2006; Tang et al. 2008, 2010).

Viral transmission as a result of change in seasons has been attributed to at least three factors. Dowell (2001) suggest extrinsically driven cycles in host resistance to infection may be caused by seasonal fluctuations in melatonin. Cannell et al. (2006) suggest that circulating vitamin D metabolites or a vitamin D deficiency may weaken human immunity. Shaman and Kohn (2009) suggest extrinsic variation such as ambient temperature and RH in the survival of the virus. It is postulated that spending more time indoors where contacts are greater causes an increase in influenza transmissibility.

Songer (1967) shows that viral sensitivity to RH appears to be an individual characteristic of a virus. For example, RSV incidence increases with rising temperature in some studies, but with decreasing temperatures in others and peaks at both a low and high temperature in different parts of the world.

Several other studies of particular note illustrate the contradictions in the data. The relationship between RSV incidence and RH is positively correlated in some studies but negatively correlated in others. Welliver (2007) shows that RSV is related to temperature with peaks of activity at high and low temperatures and at 45–65% RH while a different virus survives best at high RH and two others survive best at low RH. A study from Sweden finds no survival relationship with temperature (Linde et al. 2009). In areas with persistently warm temperature and high humidity as well as in areas where temperatures remained cold throughout the year, RSV activity was continuous throughout the year, but in temperate climates,

RSV activity was maximal during winter, correlating with lower temperatures (Thompson et al. 2003).

Many of the studies related to the effect of climatic conditions do not address factors that might critically affect the study results. For instance, the studies conducted between 1940 and the early 1960's harvested artificially aerosolized viral particles from rotating drums and then inoculated mice with uncontrolled quantities of inoculum (Wells and Henle 1941; Harper 1961). More recent studies such as those of Lowen et al. (2006, 2007a, 2007b, 2008, 2009) did not account for the distance between guinea pig cages which, had this been noted, may or may not have supported experiments by Schulman (1967,1968) in which he found a strong inverse correlation between infection rate and air exchange, regardless of whether infected and uninfected mice were physically separated. It is also significant that the Hartley strain of guinea pig used by Lowen, may not be the best animal model for investigating influenza transmission because it does not manifest typical human symptoms of influenza infection (Maher and DeStefano 2004).

Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) is a small, enveloped RNA virus that is the cause of an economically important pandemic disease in young pigs. Hermann (2007) evaluated the stability of infectious PRRSV in aerosols and derived an equation that predicts the half-life (T½) of aerosolized infectious PRRSV as a function of RH and temperature. This work verified that some airborne viruses are more stable at lower temperatures, but that viruses are not uniformly affected by environmental factors. Airborne spread of PRRSV can occur if the weather conditions are correct, i.e. low winds, high humidity, and cool temperatures.

Relative Humidity-Temperature

Arundel and Sterling (1986) conclude that RH would probably have little or no effect on the incidence of infectious diseases in environments with very high fresh air ventilation rates. Indoor contaminant levels can be exacerbated in tightly sealed energy conserving buildings with low fresh air ventilation rates. Reducing the sources of pollutants, increasing ventilation rates, or both can be used to reduce or eliminate the levels of these contaminants. In most settings where there is adequate ventilation long-range transmission does not appear to occur frequently. The ventilation rate has been shown in animal experiments to significantly affect the incidence of respiratory infections and the occupancy rate has been found in field studies to affect the number of infections during influenza epidemics. The indirect health effects of RH may be growing in importance as a result of the continuing construction of energy efficient sealed buildings with low fresh air ventilation rates. The high fresh air ventilation rates found in older leaky buildings may dilute the concentration of pathogens, allergens, and noxious chemicals in the indoor air and thus offset some of the health problems associated with RH as noted by Schulman and Kilbourne (1962).

The terms "higher RH" and "lower RH" are arbitrary. There is no experimental evidence defining a discrete demarcation of any particular RH. Studies have examined artificially aerosolized viral survival in a wide range of RH from 15% to 90% with results indicating the extreme variability in survival and infectivity. It is generally accepted that viruses with lipid envelopes such as influenza, RSV, and herpes viruses, are more stable at lower RH while other studies show that non-lipid enveloped viruses such as respiratory adenoviruses and rhinoviruses survive longer at higher RHs (Hermann 2007; Harper 1961; Schaffer et al. 1976; Ijaz et al. 1985; Karim et al. 1985; Arundel and Sterling (1986) and Cox 1989, 1998). Schaffer et al. (1976) found a more complex biphasic relationship between airborne influenza virus survival and poliovirus, a non-enveloped virus that survived longer at both high and low RH. Again, size of the aerosol particles was not accounted for in this study but the effect of a temperature of 21°C changed the viral survival rate at higher RH levels.

The interaction between temperature and humidity on viral activity is very difficult to assess. A comparison is made between a study by Harper (1961) and the Lowen and Mubareka (2007a, 2007b, 2008, 2009) studies. Harper examined in-vitro survival of four cultured viruses in aerosol, at temperatures ranging from 21°C (69.8°F) to 24°C (75.2°F). Lowen and colleagues used 20 different combinations of low, medium, and high temperature and RHs between 20–80%. Hanley & Borup (2010) made a comparison between several of these different in-vitro aerosol survival studies at different combinations of low, medium, and high temperatures and RHs between 20–80% in an effort to identify a trigger point for changes in transmission of the virus between infected and control guinea pigs. There were statistically significant differences between study results at intermediate RHs. The reason for this phenomenon has not been scientifically substantiated. The differences in survival through the range of RHs may be due to cross-linking reactions occurring between the surface proteins of these viruses (Cox 1989, 1998). However, this has not been scientifically substantiated as of this writing.

Numerous researchers, including Schaffer et al. (1976), Shephard and Shek (1998), Harper (1961), and Hemmes et al. (1960), suggest that three mechanisms could potentially explain the observed influence of RH on transmission. First, RH may act at the level of the host. Breathing dry air could cause desiccation of the nasal mucosa, leading to epithelial damage and/or reduced mucociliary clearance, which would in turn render the host more susceptible to respiratory virus infections. Long-term exposure to dry air is likely to affect influenza virus growth in the upper respiratory tract and may indeed play a role in influenza seasonality. The mucociliary clearance apparatus is an important defense mechanism for clearing the lung of foreign particulate matter. Secretory cells produce mucus that line airway passages and afford protection from disease, etc. (Bennett 2002). Pollutant exposure and viral or bacterial infections may cause disruption of mucociliary

clearance (Mubareka et al. 2009) and likewise affect the natural rheological properties such as the adhesiveness of nasal mucus and/or slowing of ciliary beating according to Salah et al. (1988).

An interesting review by Hanley and Borup (2010) regarding the atmosphere in airplanes discusses the complexity of transmission risk in that closed environment. The influenza contagion space relative to temperature and RH on aircraft is mostly unknown since studies have not been done below 20% RH. Particularly during in-flight time, RH may be between 3% to 15%. It is not known how such extremely low RH affects transmission. Dry air breathing results in mucosal water loss which consequently changes the mucosal clearance rate.

The second mechanism is that RH may act at the level of the virus particle. As previously discussed, the stability of influenza virions in an aerosol has been reported to vary through a range of RH. The third mechanism is when RH acts at the level of the respiratory droplet. At low RH, evaporation of water from exhaled bio-aerosols occurs rapidly, leading to the formation of droplet nuclei. Conversely, at high RH, small respiratory droplets take on water, increase in size and settle more quickly out of the air. As with most of the theories of aerosol transmission, a combination of these factors is probably involved.

Absolute Humidity (AH)

Few studies have examined the effect of AH on viral transmission. Although RH can be biologically significant for some organisms, it does not provide a fixed measure of atmospheric water vapor content. AH is the actual atmospheric water vapor content which for some disease systems can have greater biological significance than RH. Shaman and Kohn (2009) suggested that virus transmission was more closely correlated to AH than RH. They analyzed Lowen's data (2007a, 2007b, 2008) from guinea pig influenza transmission experiments, then converted RH values to AH values. Their findings suggest that vapor pressure exerts a much stronger control on airborne influenza virus transmission rates than either temperature or RH. The findings indicate that influenza virus transmission responds to the amount of water vapor in the surrounding air (i.e., AH), and not how close that air is to saturation (i.e., RH).

Recently, the findings related to AH were challenged with yet another contradiction. A study that examined the effect of climate factors on the seasonal incidence of influenza A, B, and RSV in the subtropical climate of Hong Kong, showed that influenza A and RSV incidence increased with higher environmental RH, whereas influenza B incidence decreased with higher environmental temperatures. Other climate variables, including vapor pressure as a measure of AH, were not significantly related to the incidence of these respiratory viruses (Tang et al. 2010).

It is important to examine RH in relation to human thermal comfort. That relationship has not been researched thoroughly in the context of humidity and dew point. Dew point is the temperature at which water condenses. The dew point is associated with relative humidity. At a high RH the dew point is closer to the current air temperature. An RH of 100% indicates the dew point is equal to the current temperature and the air is maximally saturated with water. When the dew point remains constant and temperature increases, RH will decrease. For example, at 18.3°C (65°F) dew point, the atmosphere feels sticky. The worst condition for a human is a high dew point of greater than 18.3°C (65°F) combined with high RH whereas the best condition for a human is a 15.6°C (60°F) dew point and an RH of 50–70% at 23.9°C (75°F).

CONCLUSIONS

As early as 1958, Popper noted that there is data in support of every hypothesis (for viral transmission), yet none of the hypotheses has been subjected to tests that are rigorous enough to reject it. It appears from the evidence in the literature this still holds true.

There is no conclusive evidence that any single factor, whether it be a specific temperature, RH, or geographic location can be universally applied to the wide variety of infectious viruses to reduce airborne or contact transmission, but there is pervasive evidence in the literature that the survival of viruses and other infectious agents depends partially on levels of RH. Despite a significant body of work investigating the survival characteristics of influenza in air and on surfaces, there is insufficient evidence to say that by maintaining an enclosed environment at a certain temperature and at a certain RH, this is likely to reduce the airborne survival and therefore transmission of influenza virus when compared with a similar environment that does not adhere to such a tight control of their indoor temperature and RH (Tang 2009). Although extremely low and extremely high RH have both been shown to reduce survival, these extremes were outside the conditions that would have practical application from a patient and staff comfort viewpoint in the hospital ward. The data suggest that although some changes in the rate of survival could be achieved, it probably does not justify changes to building management.

Researchers continue to investigate the complex relationship between the virus, temperature, and the amount of water vapor in the air. Most of the reported literature reviews note that findings from studies are not always consistent, though there seems to be some general indication that temperature and RH will always interact to affect the survival of airborne viruses in aerosols.

Since influenza is one of the major concerns in causing pandemics, much of the research surrounding aerosol transmission revolves around environmental effects on the influenza virus. Most of the literature shows that influenza is transmitted primarily through close contact, such as during exposure to large respiratory droplets, direct contact from hands to mouth, and short-range exposure to infectious aerosols. However, the

relative contribution and clinical importance of each of these modes is unknown.

Observational and animal studies suggest airborne transmission via small particle aerosols, but there are little data to support airborne transmission over long distances or prolonged durations of time. Most of the studies to date have not been well controlled including some of the most recent mouse and guinea pig studies. The methods used may not represent nor be compatible with natural human to human transmission. Although studies have shown that artificially generated airborne aerosols can cause infection and stay viable for varying amounts of time under varying environmental conditions, they do not represent the natural route of transmission. The variability among strains of viruses and microorganisms also may infer that their response to specific environmental conditions may vary significantly from strain to strain and therefore it would be beneficial if not practical to have controlled studies available for each strain.

The fact that significant outbreaks are relatively uncommon in acute care settings suggests that most influenza transmission occurs via large droplets. Although the general conclusions regarding indoor humidity levels suggest that at higher humidity levels and temperatures viruses do not survive as well as at lower humidity's and cooler temperatures, the evidence suggests that there are some infectious viruses that are able to survive at very low RH.

From the evidence presented, there are a multitude of factors involved in the spread of infectious disease. Most importantly among these are aerosol and droplet transmission dynamics, the nature of the dust levels, the health and condition of individuals naso-pharyngeal mucosal linings, patient susceptibility, the population density in a particular location, and the ventilation of the location.

Since no single factor is responsible for the spread of infectious viral disease, it is very important to perform a risk assessment for how the facility will be used before recommending that humidity and/or temperature be raised or lowered. In an attempt to control humidity levels in the patient and health care environment, we need to find a balance between reduced infectious disease transmissibility, levels of condensation, and patient comfort.

There is a need to examine the survival of airborne viruses in a standardized laboratory model with a repeatable methodology. It is encouraging that more experiments are being performed with human volunteers or taking place in real health care environments where humans are the main sources of such potentially infectious aerosols (Xiao et al. 2004; Fabian et al. 2008; Huynh et al. 2008; Blachere et al. 2007; Stelzer-Braid et al. 2009). These studies all differed in the way that they collected the exhaled or airborne viruses, so these factors will also need to be standardized in order to develop useful and reliable infection control recommendations based on these air-sampling results.

Future recommendations for controlling environmental conditions to reduce infectious virus transmission will need to take into account the comfort of patients and staff and importantly, length of patient stay. Although high temperatures at relatively high RH may reduce the survival of airborne influenza virus, the tolerance of people coexisting in such conditions will also need to be considered.

Also, because different airborne infectious agents (i.e. viruses, bacteria, and fungi) will have differing conditions under which they may be optimally suppressed, it will need to be decided which airborne pathogen poses the most risk to patients and staff alike. Such prioritization will be required when specific environmental recommendations are made for health care premises.

Additionally, individual level interventions such as specific vaccinations and wearing personal protective equipment are available to protect staff and patients against airborne pathogens (Jefferson et al. 2008). A combination of these methods, adapted to specific situations as required, will be used to control the transmission of airborne infectious agents. Yet the basic research to obtain the data on which these policies will depend is still far from complete.

APPENDIX: HEALTH CARE ASSOCIATED INFECTIONS

Ninety percent of all health care associated infections (HAI) are caused by bacteria, whereas mycobacterial, viral, fungal, or protozoal agents are less commonly implicated (Jain and Singh 2007). A HAI is one that develops in hospitalized patients, generally after 48 h of hospital admission and is neither present nor in incubation at the time of admission. Experience and surveillance data support the notion that the longer an individual stays in a hospital setting, the more prone that person is to acquiring an infection. However, none of the studies to date have taken "duration of patient stay" into account.

There is no clinical evidence or research that shows any correlation between a minimum level of humidity and hypothermia or wound infections in short-stay patient spaces. RH and temperature do impact environmental survival and transmissibility of select microorganisms, such as *M. tuberculosis* and influenza virus, but these fall predominately in the realm of those agents that are transmitted in settings far removed from an operating room or other anesthetizing locations. The experimental evidence indicates that even bacteria within the same structural classification (e.g., Gram-negative) may vary in how they respond to temperature and RH. Perhaps even more so than with studies on the airborne survival of viruses, the structural variation of potentially airborne bacteria may preclude useful generalizations to be made and individual bacteria may need to be considered separately when investigating their airborne survival.

Regarding Surgical Site Infections (SSIs), CDC (1999) points out that these are mostly caused by bacterial strains such as *Staphylococcus aureus,* coagulase-negative staphylococci, *Enterococcus s*pp., and *Escherichia coli* with an increasing proportion of SSIs caused by antimicrobial-resistant pathogens,

such as methicillin-resistant *S. aureus* (MRSA), (Schaberg et al. 1991; Schaberg 1994) or by *Candida albicans* (Jarvis 1995). The source of most SSI pathogen(s) comes from the patient's skin, mucous membranes, or bowel and rarely from any other endogenous source in the body. Exogenous sources of SSI pathogens are occasionally responsible for SSIs and may originate from members of the surgical team (e.g., hands, nose, or other body parts), contaminated surfaces in the operating room, the air, contaminated instruments, surgical gloves or other items used in the surgery (CDC 1999; JHU Infection Prevention Guidelines). Exogenous organisms are primarily aerobic staphylococci or streptococci species. Although fungi are widely present in the environment, they rarely cause SSIs. Viruses are not implicated in SSIs. Although it is presumed that humidity affects the viability of bacteria in the environment there are few conclusive studies that support this. As is the case for other microorganisms, bacterial viability may be affected by the bacterial coat, surrounding organic material and the host defenses of the patient.

An extensive review of the literature provides little if any evidence that a lower limit of RH as originally proposed has any impact on the frequency of SSIs. The minimum humidity level of 30% RH is a hold-over from the days of flammable anesthesia when there was a 50% RH requirement. Lowering the RH from 30% to 20%, particularly in spaces such as ORs and other short term stay areas, when combined with a thorough site-specific risk assessment might be appropriate and will certainly be more cost effective and perhaps more comfortable for the occupants. However, because the primary concern is the safety of the patient and the mitigating risk of SSI, we anticipate this review will reassure infection preventionists, clinicians, and facility engineers that a lower RH carries little if any additional risk to the patient. If, as intended, local circumstances require dropping below 30%, the evidence indicates there is also little, if any, compromise to fire safety practices and no ill effects to staff or equipment.

There have been no reported or documented cases of static electricity being an issue in providing safe environments for patients. Databases from FDA's Manufacturer and User Facility Device Experience (MAUDE) report (FDA 2011) and Emergency Care Research Institute (ECRI) have been reviewed with no incidence of equipment malfunction or fire due to static discharge.

Since the evidence clearly shows that no single factor is responsible for the spread of infectious disease, whether it be viral or bacterial, it is very important to perform a risk assessment for the use of the facility before recommending that humidity and/or temperature be raised or lowered. In an attempt to control humidity levels in the patient and health care environment, we need to find a balance between reduced infectious disease transmissibility, levels of condensation, and patient comfort.

There is insufficient evidence to state unequivocally that if a health care facility space is maintained at a certain temperature and RH, the airborne survival and transmission of influenza virus will be reduced when compared with other hospitals that do not adhere to such a tight control of their indoor temperature and RH.

Our conclusion from this review is that there is little if any evidence that reducing the lower limit of RH in short term patient care areas as accepted by ASHRAE Standard 170 (2008) standing subcommittee, will have any impact on increasing the frequency of surgical site infection. Although RH and temperature do impact environmental survival and transmissibility of select microorganisms, such as M. tuberculosis and influenza viruses, these fall predominately in the realm of those agents that are transmitted in settings far removed from an operating room or other anesthetizing locations. A site specific risk assessment that includes a review of local conditions is paramount to choosing the appropriate temperature and humidity for each situation.

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