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Environmental factors affecting the transmission of respiratory viruses

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Many viruses are capable of infecting the human respiratory tract to cause disease. These viruses display various transmission patterns among humans; however, they all share the ability to transmit from person to person, and their human transmissibility is influenced by the environment in which pathogen and host meet. This review aims to summarize recent and significant observations regarding the impact of environmental factors such as weather and climate, humidity, temperature, and airflow on the transmission of human respiratory viruses. Where possible, knowledge gaps that require further scientific study will be identified.

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Introduction

Viral respiratory tract infections are both ubiquitous and burdensome, accounting for many millions of lost school-days and workdays and millions more physician visits each year [1]. Although there are similarities in the clinical syndromes caused by the many viruses capable of infecting and causing disease in the human respiratory tract, they possess varying transmission patterns among humans. The mode or modes by which a virus transmits from person to person are critical to understanding how the environment in which they transmit impacts person-to-person spread. The Centers for Disease Control and Prevention (CDC) consensus definition for the modes of transmission of influenza virus is broadly applicable to other respiratory (i.e. non-vector-borne) viruses as well (Box 1). In this review, for consistency, we will adhere to the CDC terminology; thus, ‘contact transmission’ encompasses both direct and indirect transmission, while ‘airborne transmission,’ comprising both droplet spray

and aerosol modes, describes the direct inoculation of virus particles from the air into the respiratory tract without an intermediate.

Respiratory viruses display a great deal of variety not only in their virion structure and genome composition but also in their modes of transmission among humans (Table 1). For instance, evidence supports a primary role for direct and indirect contact in respiratory syncytial virus (RSV) and adenovirus transmission, while airborne routes (droplet spray and aerosol) seemed to be more important in SARS coronavirus spread. With other viruses, evidence is either contradictory or incomplete, and mode(s) of transmission are yet to be fully resolved.

Here we will review the effects of certain environmental factors on respiratory virus transmission, with an emphasis on influenza and respiratory syncytial viruses. We have referenced several large-scale surveillance studies, as well as experimentally generated data in small animal models. We will also discuss remaining uncertainties as to the relative importance of these factors, as well the possible contributions of non-environmental factors on the infectiousness and transmissibility of respiratory viruses.

Environmental factors affecting respiratory virus transmission

Temperature and humidity

Multiple hypotheses have been advanced to explain the specific effect of humidity and temperature on the pronounced seasonality of influenza and, to a lesser extent, disease caused by RSV and other respiratory viruses [18,19,20^{••},21,22]. These include changes in host behavior (for instance, more time spent indoors, in closed environments, during cold or rainy weather), changes in host defense mechanisms (such as impairment of mucociliary clearance with inhalation of cold, dry air) and changes in the virus infectivity and stability in different climactic conditions (Figure 1).

Animal models have elucidated potential mechanisms by which humidity and temperature influence human influenza virus transmission. In the early 1960s, Schulman and Kilbourne developed an influenza virus transmission model in mice. Although mouse-to-mouse transmission is relatively inefficient, they still observed a significant decrease in transmission efficiency with increasing relative humidity (RH) [23] and during summer months, even when laboratory temperature and RH were controlled during experiments [24]. Lowen *et al.* expanded

Box 1 Modes of person-to-person transmission of respiratory viruses

Contact transmission	In both modes of contract transmission (direct and indirect), contaminated hands play an important role in carrying virus to mucous membranes.
Direct transmission	Virus is transferred by contact from an infected person to another person without a contaminated intermediate object (fomite).
Indirect transmission	Virus is transferred by contact with a contaminated intermediate object (fomite).
Droplet spray transmission	Virus transmits through the air by droplet sprays (such as those produced by coughing or sneezing); a key feature is deposition of droplets by impaction on exposed mucous membranes.
Aerosol transmission	Virus transmits through the air by aerosols in the inspirable size range or smaller; aerosol particles are small enough to be inhaled into the oronasopharynx and distally into the trachea and lung.

(Adapted from Centers for Disease Control and Prevention (CDC); URL: <http://www.cdc.gov/influenzatransmissionworkshop2010/>).

upon these experiments in the guinea pig transmission model. At 20 °C, transmission efficiency of an influenza A/H3N2 isolate displayed a bimodal dependence on RH, with airborne (i.e. droplet or aerosol) transmission being maximal at 20–35% RH, poor at 50% RH, moderate at 65% RH, and absent at 80% RH. At 5 °C, transmission was overall more efficient than at 20 °C, and the relationship between RH and transmission efficiency was monotonic, with efficiency decreasing with increasing RH [25^{*}]. Transmission was abolished at high temperature (30 °C), regardless of RH [26].

Transmission of viruses via airborne routes may be affected by ambient humidity, which affects not only the virus' stability but also respiratory droplet size, as water content evaporates. In turn, droplet size influences whether the particle will quickly settle to the ground or remain airborne long enough to be inhaled into the respiratory tract of a susceptible host. For influenza virus, mathematical modeling suggests that RH is an important variable in airborne transmission of influenza virus; high RH favors removal of infectious particles both by increasing the settling of large, water-laden droplets and by hastening virus inactivation [27]. In aerosol viability experiments, adenovirus [28,29] and rhinovirus [30] were more stable at high RH; by contrast, a bovine parainfluenza virus was more stable at low RH [31], while RSV demonstrated bimodal peak stability at 20% or 40–60% RH with relative instability at 30% [32]. Influenza viruses are also generally more stable at lower RH; some studies have observed a bimodal stability similar to that seen by Lowen *et al.*, while others have not [20^{**}]. However, these

data should not be overinterpreted, as aerosol generation protocols and thus particle size and composition were not necessarily uniform across experiments.

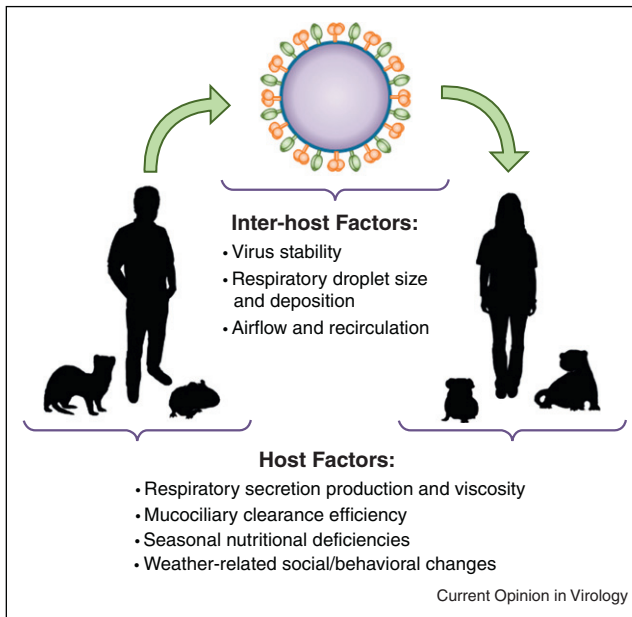
RH is a ratio that describes the actual water vapor pressure of air, relative to its vapor pressure at saturation. Because saturation vapor pressure is exponentially related to temperature, RH varies both with the temperature and with the water vapor content of air. Absolute humidity (AH), on the contrary, describes the actual water vapor content of air, without respect to temperature. Thus, at equivalent RH, warm air contains more water vapor (i.e. has higher AH) than cold air [33]. A reanalysis of the data of Lowen *et al.* showed that, although RH and temperature were both weakly correlated with influenza virus transmission efficiency, AH was strongly associated with transmission efficiency, with efficiency decreasing as vapor content of air increases [33]. Subsequent analyses of epidemiological and meteorological data in temperate areas in the United States [34] and Japan [35] suggest that low AH correlates strongly with the onset of influenza epidemic activity, more so than RH.

However, as Tamerius *et al.* observe [20^{**}], hypotheses correlating AH and influenza epidemics are best suited to explain the seasonality of influenza virus transmission in temperate climates. While influenza virus transmission has been thought not to display marked seasonality in the tropics, accumulating data suggest that equatorial regions can experience not only year-round transmission (such as Colombia; 4°N) [36] but also distinct annual epidemics that are unimodal (Fortaleza, Brazil; 3°S) or bimodal

Table 1**Modes of transmission of several human respiratory tract viruses**

Virus	Family	Primary mode(s) of respiratory transmission
Adenoviruses	<i>Adenoviridae</i>	Contact, possibly droplet spray and/or aerosol (limited data) [2–4]
Influenza viruses	<i>Orthomyxoviridae</i>	Contact, droplet spray and/or aerosol (conflicting data) [5 [*] ,6,7 [*] ,8,9 ^{**}]
Human parainfluenza viruses (HPIV)	<i>Paramyxoviridae</i>	Uncertain (limited data) [10–12]
Metapneumovirus	<i>Paramyxoviridae</i>	Uncertain (limited data) [2]
Respiratory syncytial virus (RSV)	<i>Paramyxoviridae</i>	Direct and indirect contact [7 [*] ,13], possibly droplet spray [14]
Rhinoviruses	<i>Picornaviridae</i>	Contact, droplet spray and/or aerosol (conflicting data) [7 [*] ,15]
SARS coronavirus	<i>Coronaviridae</i>	Droplet spray and aerosol [2,4,16], possibly contact [17]

Figure 1



Environmental Modulation of Respiratory Virus Transmission. Transmission of respiratory viruses depends upon a complex chain of events occurring between infected and susceptible hosts, including naturally infected humans and experimentally inoculated animals like guinea pigs and ferrets. Environmental factors such as temperature, humidity, weather, and ventilation are hypothesized to have an impact on various aspects of the transmission chain.

(Singapore; 1°N) [20^{••}]. In other tropical areas, influenza epidemics correlate with the rainy season, when AH is highest (such as Dakar, Senegal; 14°N [37], or Belem, Brazil; 1°S [38]). The question remains to what extent the seasonality (or lack thereof) of influenza epidemics is attributable to seasonal factors like humidity and temperature, what other environmental or seasonal variables matter, and which variables are causative and which are merely correlated or even confounding [20^{••}].

Precipitation

Another environmental factor that may influence viral transmissibility is precipitation. Several large-scale studies have been conducted in tropical and equatorial countries in order to determine the relationship between rainfall and respiratory disease, particularly that associated with RSV and, to a lesser extent, influenza virus. A 3-year study of RSV infections in Lombok, Indonesia (8°S) found an association between rainfall and RSV hospitalizations; interestingly, total monthly precipitation was less important than the number of days on which it rained [39]. In a study from 1982 to 1997 in Malaysia (4°N) involving over 5000 children, Chan *et al.* also documented a significant correlation between number of rainy days and RSV infection [40]. An association between rain and RSV infection has also been seen in several other studies [41–44]. By contrast, a large, 3378-children study in

Northern Taiwan (23°N) did not find any association between rainfall and RSV infection [45^{••}], nor did a 2002 study in Santiago, Chile (33°S). Of note, however, the Chilean study focused on cases in just one public pediatric hospital [46]; it is possible that a limited sampling of cases in only one hospital would hinder the ability to draw statistically significant conclusions. However, studies in other locations have found the relationship between RSV disease and rainfall to be inversely related. In a 24-month study of over 1000 symptomatic children in India (22°N), RSV infection rates were negatively correlated with millimeters of rainfall; these findings were statistically significant [47].

Inconsistencies in the role that rain plays in infection rates is not altogether surprising; discrepancies can even be reported within a given country. Following a 43-month study in Fortaleza (3°S), in the northeast of Brazil, an association between rainfall and RSV infection was documented [48]; Nascimento-Carvalho *et al.* reported a similar correlation in Salvadore (12°N) [49]. However, RSV infection did not correlate with the rainy season in Sao Paulo (23°N) [50]. While these studies employed varying techniques and collected samples over different time periods, it is possible that rain plays a unique role in RSV infection depending on a variety of factors, including geographic location. In addition, weather-dependent behavioral factors such as crowding following rainfall could also influence RSV infection rates [51], as RSV is thought to transmit through direct or indirect contact [7[•]]. Indeed, family structure, living conditions and person-to-person contact are risk factors for RSV infection [51,52].

Epidemiological data appear generally to support a relationship between influenza virus infection and rainfall. In a two-year study, a significant association was found between rainfall and influenza A virus infection in India (22°N), with little to no reported infections during the dry season [47]. These findings are in agreement with earlier studies by Rao and Banerjee, who reported a statistically significant association between rainfall and influenza virus infection, though the relative contribution to influenza A or B virus infection was not determined [53]. While it has been noted that peak influenza virus activity coincided with the first rainfall in Chennai, India (13°N) [54], the study lacked sufficient statistical rigor to determine if a relationship in fact exists. In a fairly limited study of pediatric influenza virus infections in an urban slum in Bangladesh (23°N) in 2007, 77% of the influenza B cases occurred during the monsoon season (July to September); conversely, 70% of the influenza A cases occurred during the pre-monsoon period (April to June) [55]. This study also did not determine statistical significance, and has several limitations in the study design, including the retrospective collection of samples from children who displayed clinical symptoms.

Like RSV, influenza virus transmission may be more affected by rainfall in one geographic location than another. When comparing incident influenza and weather trends in Singapore (1°N), Hong Kong (22°N), Ulaanbaatar (47°N), Vancouver (49°N), Brisbane (27°S), Melbourne (37°S), and Sydney (33°S) from 2000 to 2007, rainfall was not significantly correlated with infection [56]. Murray *et al.* reported that influenza A/H5N1 infections in Egypt (26°N) were negatively correlated with precipitation between 2006 and 2008, as the peak incidence of human infections coincided with an average of 0.2 mm of rainfall [57]. These results were not statistically significant, probably owing to the small number of human cases during the study period. In the same study, Murray *et al.* did not find any association between H5N1 infection and rainfall in Indonesia, though the authors attributed this result to variation in climate across the country, societal differences that may affect how poultry is handled, or differences in susceptibility of the inhabitants and/or poultry due to previous exposures [57].

Much less work has been done to assess the relationship between precipitation and infection with other respiratory viruses. In a study that investigated the seasonal patterns of viral and bacterial infections among hospitalized children with radiologically diagnosed pneumonia in Salvadore, Brazil (12°N), adenovirus infection was significantly correlated with total precipitation. However, parainfluenza virus infection was inversely correlated in the same study [49]. Indeed, there are substantial knowledge gaps as to how rainfall affects transmission of respiratory viruses. The effects of rain would be difficult to examine experimentally, such as in a small animal model, and it is possible that weather-related or climate-related factors other than precipitation affect seasonal infection rates.

Airflow and ventilation

Though relatively few data exist, airflow (the speed of air currents flowing through indoor spaces) and ventilation (the degree of mixing between indoor and outdoor air) seem to play a role in respiratory virus infectivity and transmission. Schulman and Kilbourne again made prescient early observations of the effect of airflow on the transmissibility of influenza viruses in the mouse model, demonstrating that the rate of transmission decreased with increasing ventilation of a closed chamber in which mice were housed [23]. A similar phenomenon was observed with rhinovirus; the probability of detecting airborne picornavirus RNA in office buildings was directly correlated with the carbon dioxide (CO₂) content of the air, which is in turn inversely related to ventilation with fresh outside air [58]; however, there were too few positive nasal samples to correlate CO₂ content with actual human infection.

Although inadequate ventilation has been implicated in the airborne transmission of respiratory viruses [59,60], the Severe Acute Respiratory Syndrome (SARS) corona-

virus outbreak in 2002–2003 provides an interesting case study for the outdoor airborne transmission of a viral respiratory pathogen. More than 300 residents of the Amoy Gardens high-rise apartment complex in Hong Kong were infected with the virus, in a dispersion pattern consistent with a single index patient, a visitor to the complex. The index patient was found to have extremely high viral loads in fecal and urine samples; computational fluid-dynamics modeling of the dispersion plume was most consistent with transit of virus aerosols through improperly sealed plumbing U-traps, up an airshaft in the index building, and then along prevailing winds into neighboring buildings up to 60 m away [61,62]. In the largest nosocomial SARS outbreak in Hong Kong, 17 of the 30 infected patients were housed in different multi-bed wards from the index patient. A recent reanalysis of this outbreak found that, even though the patient wards were designed to be at positive pressure relative to the hospital corridor (thus preventing bioaerosols from entering the wards), small differences in temperature – as little as 0.5 °C – between corridor and wards was sufficient to allow two-way airflow at ward entrances, thus permitting SARS coronavirus entry into patient wards [63].

Conclusions

Viral infections of the respiratory tract are common acute illnesses among humans, and virus transmission, by either direct or indirect routes, occurs in disparate regions around the globe. A more detailed understanding of how these viruses transmit can have broad public health implications. Indeed, a variety of meteorological factors have at times been associated with rates of virus infection as well as transmission among individuals. As presented in this review, precipitation, humidity, temperature, and airflow can be determinants of virus infection and transmission; however, despite robust investigation of the effects of these environmental factors, inconsistencies and uncertainties in the data remain. It is possible that meteorological determinants play greater roles in some geographic regions than others, or simply that differences in experimental design affect outcomes and data interpretation. Non-environmental effects, including but not limited to seasonal changes in behavior, family and social structures, and pre-existing immunity, could also be playing a role in respiratory virus transmissibility and rates of infection. Discrepancies in collected data suggest that more vigilant surveillance over large geographic regions and further controlled experiments in animal models and perhaps in humans will probably be necessary to determine with increased certainty the role that environmental factors play on the transmission of viral pathogens.

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