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Influenza and humidity — Why a bit more damp may be good for you!

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Summary Influenza viruses cause much winter-time morbidity and death in temperate regions. We still do not understand why 'flu is more common in winter. Since the 1960s, investigators have studied the role of relative humidity and temperature on viral survival, transmission and infection rates but results have demonstrated only inconclusive trends. Over the past few years however, a series of exciting studies have instead focussed on absolute humidity and demonstrated highly significant correlations with viral survival and transmission rates in both laboratory and epidemiological models. Here we review the evidence for a causal association between absolute humidity and 'flu transmission and outline how this could lead to a new approach to curbing this and perhaps other viral epidemics in the winter months.

Influenza

Influenza viruses are among the most common causes of human respiratory infections and cause high morbidity and mortality. In a typical endemic season, influenza results in approximately 200,000 hospitalizations and 36,000 deaths in the United States alone.[1] Globally, influenza A virus (IAV) is estimated to cause 3–5 million cases of severe influenza illness annually resulting in 250,000–500,000 deaths.[2] Influenza A viruses have mutation rates ranging from approximately 1×10^{-3} to 8×10^{-3} substitutions per site per year.[1] Gradual antigenic drift of surface antigens is the main driver of seasonal epidemics.[3] In contrast, influenza pandemics occur when a novel virus jumps to humans from an avian or mammalian host.[4] Creating enduring immune protection, either naturally or through vaccination to these evolutionarily dynamic viruses is therefore challenging. Furthermore, there has been limited success with achieving good coverage of annual 'flu vaccination programmes, although this is improving in some countries.[2,5] Alternative or adjunctive approaches to curbing the transmission of influenza are therefore of potential interest and importance.

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Influenza transmission

There are four main suspected transmission modes for influenza A, described in a review paper by Brankston et al.[6] and summarised below:

a) Direct contact: physical contact between infectious individual and a susceptible person.
b) Indirect contact: via inanimate objects (fomites) such as door handles, utensils etc.
c) Droplet: via large droplets ($\geq$5 μm diameter) generated and propelled through the air by coughing and sneezing into the upper respiratory tract of the susceptible recipient.
d) Airborne: via aerosolization in air borne virus-containing droplet nuclei ($<$5 μm diameter) resulting from evaporation of larger droplets or dust or cellular material. Suspended in the air for long periods and dispersed by air currents, droplet nuclei may be inhaled by susceptible hosts.

The relative importance of each transmission mode continues to be debated with a growing consensus that the main modes of influenza transmission are the droplet and both direct and indirect contact routes.[6]

The seasonality of influenza

In temperate regions of the world, influenza epidemics are more common in the winter.[7]

There are three main competing but not mutually exclusive hypotheses which seek to explain this[8]:

1) Reduced host immunocompetence, for example due to reduction in vitamin D levels and melatonin in the winter.[9–11]
2) Changes in host behaviours such as increased contact between individuals in indoor spaces, for example at the start of and during a school term.[12]
3) Changes in environmental conditions such as air humidity and temperature. These might affect infection rates either through effects on the host (for example the integrity or function of the upper respiratory mucosa) or on the infecting agent by changing virus viability or efficiency of transmission.[8]

The evidence for the first two hypotheses has already received some research attention and it appears possible that both have some effect on influenza transmission. However they do not appear fully to explain the seasonality observed. The focus of this paper will be around how humidity may influence 'flu epidemics.

Relative and absolute humidity

When we consider humidity we generally think in terms of relative humidity (RH); this is the amount of water vapour present in air, expressed as a percentage of the amount needed for saturation at the same temperature. RH affects how hot we feel at a given temperature by altering the effectiveness of sweating as a cooling mechanism. In high RH, sweat does not easily evaporate because the air is already nearly completely saturated with water. Heat is therefore not lost, leading to continued but ineffective sweating. At cloud level, RH also determines whether it will rain.

Absolute humidity (AH), also known as vapour pressure, and measured in millibars (mb), is the total water content of the air; it can be calculated by dividing the mass of water vapour by the mass of dry air in a volume of air at a given temperature. Crucially, the hotter the air, the more water it can contain so that much higher AH is achievable in warm conditions than in cold. When it is cold, the air often feels humid: the RH is high, but the amount of water in the air – the AH – is low, as cold air cannot carry much water.

Low absolute humidity and increased rates of influenza transmission in animals

Several attempts have been made to evaluate the effects of changing environmental factors including temperature and RH on the transmission of 'flu in laboratory animals.[13,14]

Lowen et al. used guinea pigs as their influenza transmission model to investigate how different temperature and RH conditions affected rates of transmission. Guinea pigs are reported to be good models for influenza transmission.[15] These authors showed a relatively weak inverse association between RH and viral transmission.[14,16]

There had not been any studies of the effect of AH on influenza virus transmission (IVT) until Shaman and Kohn used the data published by Lowen et al. to recalculate AH from the RH and temperature values and model its effect on IVT and influenza virus survival (IVS). Based on the observation that there a strong seasonal cycle in AH, both outdoor and indoor, with lowest values during the colder winter months in temperate regions, they hypothesised that AH was more likely to affect viral survival and transmission than RH which is often high in the winter. Using linear regression to plot temperature, RH and AH against IVT they demonstrated that AH had a highly significant inverse relationship ($p = 0.00027$) with viral transmission; i.e. the lower the AH, the more viral transmission occurred. The statistical significance of this was much greater than for RH and IVT as well as temperature and IVT (see Fig. 1).[17] To date, there are no trials investigating the effect of humidity on the rates of influenza transmission in humans.

Relationship between influenza virus survival and absolute humidity

Like transmission, IVS has been investigated at different levels of RH and temperatures, once again showing correlation trends of borderline significance.[18] A similar reanalysis, substituting RH with AH values, produced a clearer, nonlinear relationship between IVS and AH (Fig. 2).[17] The authors discuss the fact that a more comprehensive series of laboratory investigations at various AH levels are needed in order to validate and explore further the relationship between IVT and AH and whether this is also non-linear. The