

## HYPOTHESIS

### Impact of Atmospheric Dispersion and Transport of Viral Aerosols on the Epidemiology of Influenza

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Current theories of influenza viral epidemiology have not explained the persistence, seasonality, and explosive outbreaks of virus over large geographic areas. It is postulated in this paper that atmospheric dispersion and intercontinental scale transport of airborne aerosolized influenza virus may contribute to the spread, persistence, and ubiquity of the disease, the explosiveness of epidemics, and the prompt region-wide occurrence of outbreaks and that seasonal changes in circulation patterns and the dispersive character of the atmosphere may help to explain the regular annual cycle of influenza activity.

The current epidemiologic concept of influenza viral infections parallels the measles model, in which it is believed that infections are spread by direct serial transmission from person to person, principally by the microscale dispersion of viral aerosols [1, 2]. While we recognize that direct serial person-to-person spread is likely the usual mode of transmission of influenza virus, this theory does not adequately explain either the persistence of the virus as a human pathogen or the seasonality of outbreaks [3]. It also fails to account for other influenza characteristics, such as ubiquity, explosive outbreaks, the prompt region-wide occurrence of epidemics, and the relatively constant pattern of influenza epidemics over several centuries [4].

#### Hypotheses

We hypothesize that long-range atmospheric transport of aerosolized influenza virus may contribute to the spread and persistence of influenza virus and that seasonal changes in atmospheric circulation patterns and dispersive characteristics may lead to the regular annual cycles of influenza activity. The following evidence is presented in order to demonstrate the feasibility of these hypotheses.

*Intercontinental transport of aerosols.* Aerosols

are dispersed vertically through the depth of the planetary boundary layer (typically 100–1,500 m) by mechanically and thermally induced turbulent mixing and are dispersed horizontally over tens to hundreds of kilometers by the low-level winds [5]. Aerosols caught up in deep convection or in air flowing up through low pressure centers with frontal waves are conveyed to the upper levels of the atmosphere. They may then be transported hundreds to thousands of kilometers before being returned to the surface [5]. The coarse particles become condensation nuclei for rain droplets (rain-out) and are collected by falling rain droplets (wash-out). They are also removed by sedimentation and by impaction (dry deposition). However, accumulation-mode particles (0.1–3.0  $\mu$  in diameter), which include the vast majority of the  $10^4$ – $10^6$  particles that may be produced by each cough or sneeze [6], are too small to be effectively removed by wet and dry deposition. Aerosol particles of this size remain airborne for a few days to a few weeks [7] before returning to earth with air subsiding in a high-pressure center, with air sharply sinking near a cold front or with other forms of downdraft.

Considerable evidence for the long-range transport of aerosols by the atmosphere has been collected, mainly from satellite images and from meteorologic back-trajectory analysis along with chemical "fingerprinting." Such evidence includes the facts that (1) aerosol dust, originating in China, has been transported >10,000 km across the north Pacific [8]; (2) forest fire smoke from northwestern Canada has been tracked >9,000 km to Europe [9];

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(3) radioactive fallout from the Chernobyl incident has been detected around the world [10, 11]; and (4) Eurasia has been identified as the primary source region for anthropogenic aerosol pollution in the polar regions of North America [12].

*Atmospheric pathway and dispersive characteristics.* Between Asia and North America, a potentially favorable atmospheric pathway exists that may be relevant to the spread of influenza. In winter, the southeast coast of Asia is an active frontal zone with frequent cyclogenesis, i.e., development of low-pressure centers [13]. Surface aerosols, and potentially aerosolized influenza virus, may be conveyed to the upper levels of the atmosphere by these systems. There they usually encounter a fast westerly flow that transports them towards North America. In summer the frontal zone moves northward and weakens, cyclogenesis drops off, and the upper flow becomes easterly over Southeast Asia [13]. This effectively cuts off the atmospheric pathway to North America.

Thus, it is postulated that the Far East may be a source of wintertime influenza viral aerosols that reach North America a week or two after they are emitted into the atmosphere. Seasonal changes in atmospheric circulation patterns may help to explain the absence of influenza on the North American continent in summer.

When the westerly upper-level winds, potentially transporting viral aerosols, overtake a southward-advancing wedge of Arctic air (i.e., a cold front), the air is forced to sink [14]. This often occurs over North America in the winter, when the cold polar dome of Arctic air spills southward over the continent [12]. Usually, there is a narrow band of sharply sinking air in the cold frontal zone, followed by weaker but broader-scale subsidence in a trailing high-pressure center [15]. By this mechanism, accumulation-mode-sized aerosols that have been transported eastward by the upper westerlies may be brought down to the surface. As the cold front sweeps southward, the aerosols may be spread across a broad geographic area. Potentially, influenza viral aerosols could be inhaled, causing primary infections in a number of separate locations. Given this sequence of events, the region-wide occurrence of influenza epidemics and their explosive nature would no longer be a puzzle.

Regardless of how influenza virus is introduced into the community, whether by seeding from the atmosphere or by travelers, subsequent dispersion of viral aerosols would be confined to the planetary

boundary layer, and the virus might persist in an area with stagnant nondispersive meteorologic conditions. Stagnant weather is prevalent under Arctic high-pressure centers, which typically follow cold fronts in winter, and the dispersive capability of the lower atmosphere (characterized by its daily maximum ventilation coefficient) is generally much lower over temperate North America in winter than in summer [16], a fact that might contribute further to the seasonality of influenza epidemics (perhaps already largely determined by seasonal atmospheric circulation patterns).

Only one possible atmospheric pathway for the long-range transport of aerosolized influenza virus has been discussed. However, pollution studies have identified other source-to-sink pathways within the global circulation of the atmosphere [8]. Ultimately, all of these pathways are interconnected. Thus, the entire population of the world may become exposed to airborne influenza virus. This may help to explain the ubiquity and persistence of this disease.

*Long-range airborne spread of viral infection.* Epidemiologic investigations have confirmed that the virus that causes foot-and-mouth disease has been transported by the atmosphere across the Baltic Sea [17] and across the English Channel [18]. These regional results, along with demonstrated microscale dispersion of certain viruses, suggest that, like air pollution, the airborne spread of pathogens may be a problem that extends from the local to the inter-continental scale.

*Infectivity of low-concentration viral aerosols.* Although greatly influenced by the amount of secretion in the nasal passages, a single cough or sneeze can produce  $10^4$ – $10^6$  accumulation-mode-sized particles that can remain airborne for extended periods [6]. It follows that an infected populace in a region of the Far East could constitute a significant source of viral aerosols. Long-range transport accompanied by atmospheric dispersion would inevitably lead to much lower downstream concentrations. Nevertheless, some relatively undiluted air parcels might make it across the Pacific Ocean, and the virulence of aerosolized influenza virus at low concentrations might still be sufficient to cause infections.

Influenza studies in mice have shown a greater infectivity of airborne versus intranasal inoculation of virus [19]. Knight [20] demonstrated in volunteers that influenza virus is five to 10 times more infectious when introduced by the aerosol route than by the intranasal route and that adenovirus type 4 is

70 times more infectious by the aerosol route [6]. Aerosolized influenza A virus produces illness in humans at dosages indistinguishable from one infecting particle [6].

Measurements of aerosol concentrations and size distributions made in a pristine area of Alaska [21] indicate that, on average, winter air masses with trajectories off the Pacific Ocean have 100 accumulation-mode-sized particles per cubic centimeter. Some of the aerosols entering North America may contain viable influenza virus.

*Long-term survival of aerosolized influenza virus.* In one study, the mouse LD<sub>50</sub> was similar at 20 h of aging of aerosolized influenza virus at room temperature to that at earlier times, but the effect of varying the temperature was not considered [22]. It has been shown that influenza virus is maximally stable at low relative humidity [23]. The study of a different enveloped respiratory virus has shown a pronounced stabilizing effect of low temperatures on the survival of aerosolized human coronavirus 229E, even with a high relative humidity [24]. The authors found that at 85% relative humidity, decreasing the temperature from 20°C to 6°C extended the infectious half-life of coronavirus from ~3 to 86 h. At the optimal humidity—~50%—nearly 20% of the virus was still detectable after 6 d in aerosols stored at 20°C. The viral half-life was ~70 h. Lowering the temperature to 6°C stretched the half-life to >100 h. The influence of relative humidity may be a confounding factor in assessing the stability of the infectious dose, but it appears that aerosolized coronavirus 229E—and, by implication, influenza virus—can be stable for long periods at low temperatures.

*Atmospheric conditions and the survival of influenza virus.* The observation that lowering the temperature extends the infectious half-life of coronavirus 229E suggests that some enveloped viruses might be able to survive long-range transport in the atmosphere where temperatures drop off dramatically with height. Representative values around 40° north latitude are –5°C at 3,300 m, –25°C at 6,500 m, and –44°C at 9,800 m [25]. These cold atmospheric temperatures may extend the infectious half-life of aerosolized influenza virus, enabling long-range transport of infectious virus.

The effects on the survival of aerosolized influenza virus of atmospheric humidity and its postulated role in the epidemiology of influenza infections have been noted previously [26]. In winter, temperate North

America's climate and artificial heating lead to low relative humidities indoors. This favors the survival of aerosolized influenza virus [22, 23] that may have been transported to this region and may aid in the local spread of infection.

Noteworthy, but of unknown relevance to virus survival in the atmosphere, is the observation that accumulation-mode particles, which may contain influenza virus, interact efficiently with sunlight [27]. However, the impact of selective scattering, reflection, and absorption of the various wavelengths in sunlight and ultraviolet light by aerosols varying in diameter from ~0.1 μ to 3.0 μ is unknown.

### Future Studies

In order to test these hypotheses, several activities should be considered. Influenza surveillance and epidemiology should be improved worldwide. Evaluations of meteorologic factors and influenza epidemiology in various parts of the world may reveal consistent atmospheric patterns preceding and during the spread of influenza viral infection. This may have important applications for future methods of influenza viral surveillance and detection and, potentially, of the control of influenza infections.

Influenza viral infectivity must be examined at various temperatures, as well as relative humidities, to validate the potential for long-term atmospheric survival of influenza virus.

A more detailed study of the nucleotide sequence of influenza viral genes may help to establish whether a common source of influenza virus exists, as a form of epidemiologic fingerprinting. Recent studies have demonstrated that the H1 hemagglutinin gene of influenza A virus over two eras has shown two pathways of evolution [28], and multiple evolutionary pathways have been demonstrated for the H3 hemagglutinin [29]. It would be of interest to compare nucleotide sequences of multiple strains of isolates collected within one year and from various geographic regions. Highly conserved strains might suggest the possibility of seeding or transmission from a single source (as has been demonstrated by the chemical fingerprinting method in identification of the source of various atmospheric pollutants).

An examination of historical records in areas of geographic isolation before the era of modern travel may provide support for the atmospheric origin of clinically documented influenza.

Sampling the air for the presence of aerosolized

influenza virus would be of importance in substantiating our hypotheses, although current technology may not be sensitive enough to study this in nature.

In summary, the above hypotheses and one model for possible long-range atmospheric transmission of influenza virus are intended to contribute ideas for discussion and evaluation of an important communicable disease whose epidemiology is not fully understood [3, 4].

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