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A four year seasonal survey of the relationship between outdoor climate and epidemiology of viral respiratory tract infections in a temperate climate

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ABSTRACT

Background: The relation between weather conditions, viral transmission and seasonal activity of respiratory viruses is not fully understood.
Objectives: To investigate the impact of outdoor weather in a temperate climate setting on the seasonal epidemiology of viruses causing respiratory tract infections, particularly influenza A (IFA).
Study design: In total, 20,062 clinical nasopharyngeal swab samples referred for detection of respiratory pathogens using a multiplex PCR panel, between October 2010 and July 2013, were included. Results of PCR detection were compared with local meteorological data for the same period.
Results: Low temperature and vapor pressure (VP) were associated with weekly incidence of IFA, respiratory syncytial virus, metapneumovirus, bocavirus and adenovirus but no association with relative humidity was found. The incidence of human rhinovirus and enterovirus was independent of temperature. During seasonal IFA outbreaks, the weekly drop of average temperature (compared with the week before) was strongly associated with the IFA incidence recorded the following week.
Conclusion: A sudden drop in outdoor temperature might activate the annual influenza epidemic in a temperate climate by facilitating aerosol spread in dry air. These conditions also seem to affect the incidence of other respiratory pathogens but not human rhino- or enterovirus, suggesting that routes of infection other than aerosol may be relevant for these agents.

1. Background

Worldwide, annual epidemics of viral respiratory tract infections (RTI) constitute a major health burden. Especially influenza is associated with considerable morbidity and mortality [1,2–5]. In the temperate climate zone, the seasonal appearance of influenza and other respiratory viruses is well described [6–8], yet the driving force behind this seasonal variation remains enigmatic to a large extent. Several factors that might explain the seasonality have been suggested, including antigenic drift and shift in influenza viruses, host immune response, social behaviour including indoor-crowding during poor weather as well natural occurring fluctuations of climate factors and solar-radiation [9–12]. Of particular interest is the role of meteorological factors as key players behind the marked seasonality in the temperate regions, where the influenza peak is associated with a cold and dry climate, whereas humid and rainy conditions seem to favour influenza activity in tropical regions [13].

Previous studies have shown that ambient temperature is associated with the annual influenza peak [14–16], possibly by influencing transmission and stability of the virus [17–19]. However, during the past decade, focus has shifted towards the role of humidity. Low relative humidity (RH; which describes the water content in a gas, relative to the maximum capacity of water vapor that a gas can hold, at a given temperature) has been shown to contribute to the transmission and survival of influenza virus [18–21]. The plausible explanation for this is that low RH leads to evaporation of aerosolized virus particles, allowing them to remain airborne for an extended period of time [17]. However, in the temperate climate zone, outdoor RH reaches maximum levels during

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wintertime, suggesting that the variation regarding this parameter may not fully explain seasonality.

More recent reports have investigated the role of absolute humidity (AH; the amount of water per volume unit of air (g/m^3), irrespective of temperature) and found a stronger correlation between low AH and influenza activity in temperate regions than compared to RH [22–24]. Other climate factors such as precipitation have in some studies been associated with activity of IFA and other respiratory viruses, especially in the tropics [25–28] but there is a big discrepancy in the literature concerning the role of rain on transmission of respiratory viruses [29]. Furthermore, a link between climate and the epidemiological pattern of other viruses causing RTI such as respiratory syncytial virus (RSV), human metapneumovirus (HMPV) and human coronavirus (HCoV) [30–36] has been suggested.

2. Objectives

The aim of the present study was to investigate the impact of outdoor weather conditions on the seasonal epidemiology of viruses causing RTI, using a multiplex polymerase chain reaction (PCR) panel for 16 viral pathogens during three consecutive seasons. In particular, we wanted to explore the relative influence of climate factors on the onset of the annual IFA epidemics as well as the seasonal incidence of other respiratory viruses.

3. Study design

3.1. Patient samples

This retrospective study included all clinical naso-pharyngeal swab samples collected between October 2010 and July 2013 (n = 20062), which were sent to the Department of Virology at Sahlgrenska University Hospital (a 2000 bed teaching hospital), in Gothenburg, Sweden (populated by approximately 600,000 inhabitants), for detection of respiratory pathogens by routine multiplex real-time PCR. The study population covered all age groups, including children. Samples were predominantly referred from hospital inpatients but also from primary health care facilities as well as hospital outpatient clinics. No clinical or demographic information regarding the patients were available.

3.2. PCR detection

The real-time PCR assay on nasopharyngeal aspirates (NPA) used during the study period targeted sixteen viruses and two bacteria in separate PCR systems; influenza virus A (IFA) and B (IFB), RSV, human rhinovirus (HRV), human enterovirus (HEV), human coronavirus (HCoV −NL63, −OC43, −229E and −HKU1), human metapneumovirus (HMPV), human adenovirus (HAdV), parainfluenza virus (PIV) type 1–4 and human bocavirus (HBoV), and the bacteria *Chlamydophila pneumoniae* and *Mycoplasma pneumoniae.*

All samples were analysed using the same technique. Nucleic acid from 100 μL specimen was extracted into an elution volume of 100 μL by a Magnapure LC robot (Roche Molecular Systems, Mannheim, Germany) using the Total Nucleic Acid protocol, and was amplified in an ABI 7900 real-time PCR system (Applied Biosystems, Foster City, CA) in 25 μL reaction volumes. After a reverse transcription step, 45 cycles of two-step PCR were performed. Each sample was amplified in 8 parallel reactions, each containing primers and probes specific for 2–3 targets. The method has previously been described in detail [37,38]. In cases with a positive signal for both HRV and HEV with a cycle difference of <5 cycles, indistinguishable HEV/HRV was reported. The PCR panel continuously underwent external quality assessment through QCMD (Quality Control for Molecular Diagnostics), including all agents except bocavirus and coronavirus HKU1. Boca virus was included into the panel in November 2011, otherwise no major changes of the assay were made.

3.3. Meteorological data

Data on average weekly outdoor temperature (degrees Celsius), vapor pressure (VP; hPa), relative humidity (RH, %), wind speed (m/s) and precipitation (mm) for the study period were obtained from the Swedish Meteorological and Hydrological Institute (SMHI) obtained at the local weather station in Gothenburg (5 m above the sea level, situated at Latitude: 57.7157N, Longitude: 11.9925E). As previously mentioned, AH describes the actual vapor pressure in a volume of air irrespective of temperature. Different measures in meteorology of AH include vapor pressure, specific humidity and mixing ratio. The data on humidity provided by SMHI, and used in this study, were expressed in VP (hPa).

The weekly incidence of each pathogen included in the routine PCR panel during the study period was analysed for seasonality and association with climate factors, using average weekly means of included meteorological parameters. For each of the three seasonal influenza outbreaks during the study period, we choose to further study the period from two weeks prior to the first week with average weekly temperature below zero degrees Celsius to the week with maximum IFA incidence, when analysing the onset of each epidemic.

3.3.1. Statistical analysis

We used simple linear regression analysis for univariate comparison of the weekly incidence for each virus and several meteorological parameters across all seasons. Multiple linear regression analysis, using the enter strategy, was performed with each agent as dependant variable and the climate factors as independent variables. Analysis of variance was utilized to assess the significance of each multiple regression model and a p-value of <0.05 indicated a qualified model. Data on the seasonal IFA outbreaks were also analysed with multiple linear regression to further explore the relation between the drop in temperature during the three preceding weeks and the weekly incidence. P values below 0.05 were considered statistically significant (2-sided). The statistical analysis was made using the SPSS software package version 22.0.0.0 (IBM, Armonk, NY).

4. Results

Altogether, 20062 samples were examined during the study period, of which 10579 (52.3%) were positive for one or more respiratory agent. Detection frequencies are displayed in Fig. 1. IFA, IFB, RSV, HCoV and HMPV all displayed a strong seasonal pattern peaking during the cold winter months whereas HRV was prevalent across all seasons (Fig. 2).

4.1. Meteorological factors and incidence of respiratory viruses

In the univariate comparisons, between meteorological factors (weekly averages for outdoor temperature, outdoor vapor pressure, relative humidity, wind speed and precipitation) and the weekly incidence of respiratory viruses included in the panel, the weekly incidence of IFA, IFB, RSV, HCoV, HMPV, HBoV and HAdV correlated significantly with low outdoor temperature as well as vapor pressure (except for PIV which was associated with vapor pressure only). Relative humidity correlated with the incidence of IFB, HCoV, PIV and HEV. No association between RH and IFA, RSV, HMPV, HBoV and HAdV was found. No meteorological factor was associated with HRV infections apart from a positive correlation with wind speed.