Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Clinical Virology 84 (2016) 59–63

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

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

Nicklas Sundell[a,*], Lars-Magnus Andersson[a], Robin Brittain-Long[b], Magnus Lindh[a], Johan Westin[a]

[a] Department of Infectious Diseases/Clinical Virology, University of Gothenburg, Sweden
[b] Department of Infectious Diseases, Aberdeen Royal Infirmary, Aberdeen, Scotland, UK

ARTICLE INFO

Article history:
Received 25 April 2016
Received in revised form
20 September 2016
Accepted 4 October 2016

Keywords:
Influenza A
Respiratory viruses
Meteorological factors
Epidemiology

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

* Corresponding author at: Department of Infectious Diseases, Institute of Biomedicine, Sahlgrenska Academy, University of Gothenburg. Guldhedsgatan 10b, 413 36 Gothenburg, Sweden.
E-mail address: nicklas.sundell@vgregion.se (N. Sundell).

http://dx.doi.org/10.1016/j.jcv.2016.10.005
1386-6532/

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.

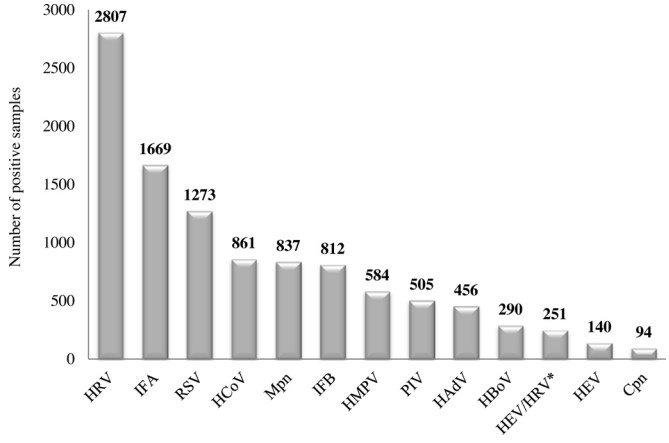

Fig. 1. Distribution of agents detected by multiplex real-time PCR in 10579 positive nasopharyngeal swab samples during the three year study period (2010–2013). IFA = Influenza A, IFB = Influenza B, RSV = respiratory syncytial virus, HRV = human rhinovirus, HEV = human enterovirus, HCoV = human coronavirus, HMPV = human metapneumovirus, HAdV = human adenovirus, PIV = parainfluenza virus, HBoV = human bocavirus, Mpn = Mycoplasma Pneumoniae, Cpn = Chlamydophila Pneumoniae, HEV/HRV* = Not distinguishable by PCR.

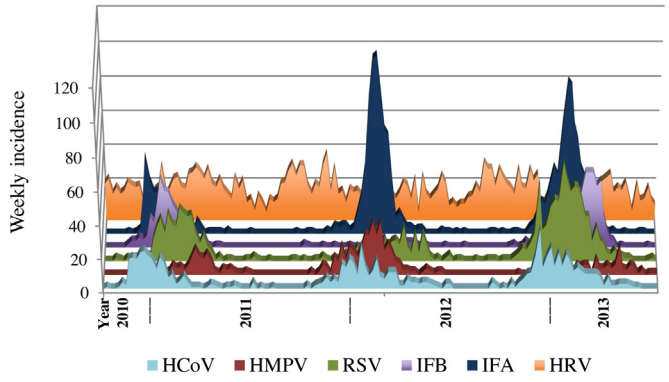

Fig. 2. Weekly incidence of various respiratory pathogens, detected with real-time PCR, according to season across three consecutive years 2010–2013 (n = 8006). All agents except human rhinovirus have a strong seasonal pattern with outbreak occurring during wintertime and almost no activity during summer.

Thus, the non-enveloped picornaviruses (HRV and HEV) differed from most of the enveloped viruses in being independent of outdoor temperature and vapor pressure.

Multiple regression analyses were performed for each agent to explore which of the weather factors were independently associated with a high incidence. Temperature correlated strongly with vapor pressure ($R^2 = 0.91$; $p < 0.0001$), and therefore it would be inappropriate to fit both of them into the regression models. Thus, temperature was chosen for further modelling and vapor pressure was left out. Temperature, relative humidity, wind speed and precipitation were included as independent variables and the weekly incidence for each agent respectively as the dependent variable. The results of the multiple linear regression analyses for all agents are displayed in Table 1.

4.2. Meteorological factors and onset of influenza A epidemic

During all investigated seasons, the start of the IFA epidemics coincided sharply with the point of time when average weekly temperature for the first time each season fell below the freezing point (0° Celsius) and average weekly vapor pressure subsided 4 hPa (Fig. 3).

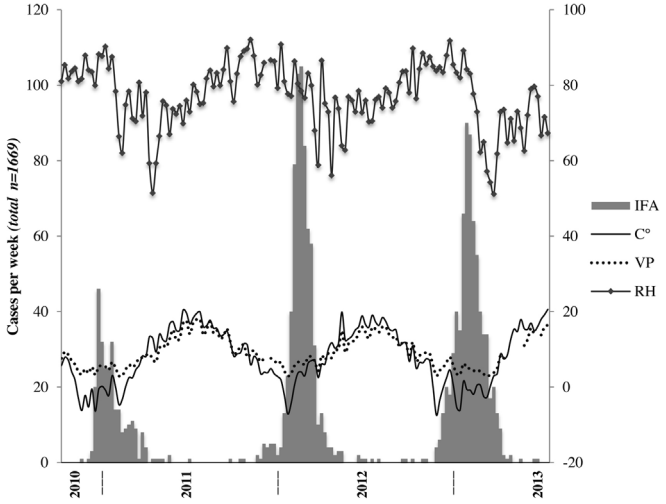

Fig. 3. Weekly incidence (number of cases/week) of influenza A (IFA) virus infections (grey bars) according to average weekly outdoor temperature (degrees Celsius; solid black line), vapor pressure (VP (hPa); dotted black line) and relative humidity (RH (%); squared black line) across the entire study period (October 2010–July 2013).

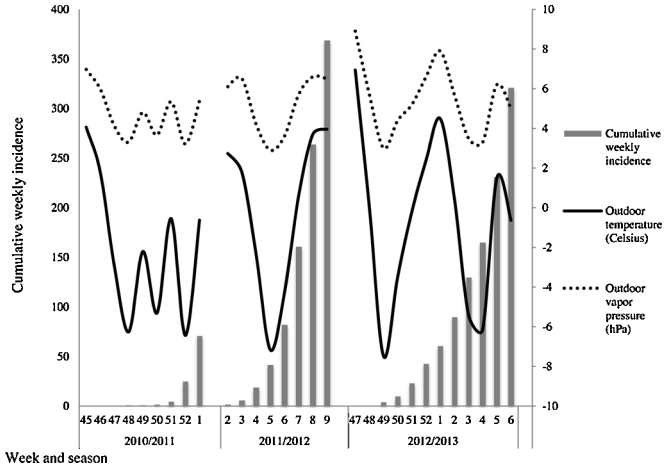

Fig. 4. Cumulative weekly incidence of influenza A (IFA) virus infections (number of cases per week; grey bars) according to average weekly outdoor temperature (degrees Celsius; solid grey line) and vapor pressure (dotted black line) during each of the three seasonal IFA outbreaks that occurred during the study period, separately.

Data on each outbreak is depicted in Fig. 4. To closer analyse the relation between the change in temperature and the onset of the seasonal epidemic, we used multivariate regression to investigate the relation between the magnitude of the weekly change in temperature (temp drop) during the three preceding weeks, and the weekly IFA incidence, during the three seasonal epidemics. Data are summarized in Table 2. There was a significant association between IFA incidence and the change in temperature recorded the week before.

5. Discussion

In our study, we investigated the epidemiological patterns of viral RTIs across three consecutive years by comparing meteorological data with molecular diagnostic test results of samples collected from more than 20,000 patients, in a temperate climate. The main finding was a strong association between a drop in temperature and the start the influenza season and that low outdoor temperature was associated with the weekly incidence of several respiratory viruses, except for HRV or HEV. We propose that reduced size of

Table 1
Multiple regression analysis showing the weekly incidence of different respiratory agents in relation to climate factors. Only significant predictors are displayed.

Agent (weekly incidence)	Significant predictor(s)	Cases (total n)	Adjusted R^2	Coefficient	*p*
Rhinovirus	Wind speed	2807	0.07	3.09	<0.0001
Influenza A	Temperature	1669	0.22	−1.23	<0.0001
RSV	Temperature	1273	0.34	−0.88	<0.0001
Coronavirus	Temperature	861	0.51	−0.65	<0.0001
Influenza B	Temperature	812	0.38	−0.86	<0.0001
	Rel humidity		0.38	−0.53	<0.0001
Metapneumovirus	Temperature	584	0.12	−0.2	<0.0001
	Wind speed		0.12	1.95	0.008
Parainfluenzavirus	Rel humidity	505	0.07	−0.1	0.008
	Wind speed		0.07	0.82	0.04
Adenovirus	Temperature	456	0.28	−0.16	<0.0001
Bocavirus	Temperature	290	0.16	−0.11	<0.0001
	Wind speed		0.16	0.76	0.008
Enterovirus	Rel humidity	140	0.08	0.44	0.001

aerosol droplets due to evaporation by reduced temperature (and vapor pressure) during cold outdoor conditions may extend the duration of time when such infectious droplets remain airborne and thus increases the chance of infecting new hosts [17].

Low temperature has been shown to increase IFA activity previously [14–16,24] and several authors have reported that cold weather precedes IFA epidemics in a temperate climate [14,15,22–24]. Multivariate analysis revealed an association between weekly incidence of influenza and outdoor temperature, independent of other weather factors and the curves displaying the weekly incidence revealed that a quick drop below zero preceded the start of the annual epidemic each of the examined seasons in our setting. Jaakkola et al. recently found that a drop in temperature during the three preceding days increased the risk for influenza virus transmission, however this study had a limited positive sample size and used daily averages. In order to further analyse the relationship between the start of IFA epidemics and climate factors we also investigated the weekly changes of meteorological parameters during outbreak and we found that alterations in temperature (and hence, vapor pressure) precedes the increase of IFA infections by one week in a similar geographical setting. This suggests that declines in outdoor temperature may be an important predictor for the IFA outbreaks, which may serve to kick-start the annual epidemic. It is important to notice that there is a relatively strong covariance between outdoor temperature and AH (expressed as VP in our study) and that they are strongly connected. We believe that both are critical for shaping conditions favourable for aerosol spread, but whether they should be considered as separate factors or as one connected entity in epidemiological models are up for further studies.

Some experimental studies have reported that low RH may affect transmission and survival of influenza virus [19–21]. Our observations suggest that AH is more strongly associated with IFA onset and activity than RH. In fact, we observed slightly higher RH during winter compared to the rest of the year, arguing against that RH would explain the marked seasonality, and this has also been questioned by reports by others [23,24]. Even though outdoor RH is higher during the winter months in temperate climate, the amount of water vapor that a unit of air can hold is significantly smaller when the temperature is low, meaning that the air is very dry in terms of AH. Indoor heating wintertime causes RH to drop heavily and creates an even dryer indoor environment that might further favour transmission of influenza viruses by reducing the size of aerosol particles through evaporation. Therefore, maintaining a higher level of humidity indoors might help reducing transmission [39].

Table 2
Multiple regression analysis showing the relation between the weekly incidence of influenza A virus and the change in average weekly outdoor temperature (temp drop) compared with the previous week at week 0 (current week), −1 (1 week ago) and −2 (2 weeks ago), during three consecutive seasonal outbreaks.

Agent (weekly incidence)	Potential predictor (s)	Coefficient	Adjusted R^2	*p*
Influenza A	*Temp drop* **week 0**	0.35	0.22	0.05
	Temp drop **week −1**	0.38	0.22	0.03
	Temp drop **week −2**	0.16	0.22	0.36

In our series, RSV peaked during late wintertime (February to March) all seasons while IFB appeared biennially. An association between climate and RSV as well as IFB has been reported previously [30–32,40–43]. Since our observation period was limited we can only conclude that IFB appears irregularly in our geographical area, which is consistent with the finding from a 10 year-surveillance conducted by Weigl et al. [6]. Our findings suggest that temperature and vapor pressure may influence activity of RSV, but also IFB once the prerequisites for an annual epidemic are fulfilled. We believe that the observed negative correlation between IFB and RH may be a coincidence. A study by Gaunt et al. found marked winter seasonality of HCoV in a similar geographic setting [35] and in the temperate climate zone HMPV also peaks during wintertime or early spring [33,36,44,45] whereas an inverse pattern has been observed closer to the equator [46]. In agreement with these reports both HCoV and HMPV activity was strongly associated with low temperature and VP in our study. PIV appeared irregularly with a single episode of high incidence in the spring of 2013. A previous study in the same geographical area also found PIV to peak during springtime [8]. We found a weaker correlation between PIV and VP compared to IFA, and we believe that PIV may be less dependent of meteorological factors. HRV and HEV appear frequently across seasons in our study. HRV have a tendency to accelerate during autumn in the temperate zone [43,47]. We speculate that infections caused by HRV and HEV, which are non-enveloped viruses and therefore more robust than most of the respiratory viruses, may be transmitted via large droplets or close contact rather than via small-aerosolized particles and therefore be less dependent on climate factors for spread. The association between HRV incidence and weekly average wind speed should be interpreted with caution since weekly average may be a suboptimal way to quantify the impact of wind. It could however reflect increased transmission due to indoor crowding during longer periods of windy climate.

Our study has several limitations. Although the relatively large sample size have been analysed at the same laboratory, a few specimens were collected as far as 100 km from the laboratory. Any differences in temperature and humidity are likely to be small within this geographical area and we believe that this factor would

not change our findings in any substantial way. We choose to study weekly averages in temperature and humidity, in order to exclude the risk of the turbulence given by the swift alterations that may occur on a daily basis. The number of seasons included in this study was too few to justify the use of monthly averages.

In conclusion, our results suggest that a sudden drop in outdoor temperature might activate the annual influenza epidemic in a temperate climate by facilitating aerosol spread in dry air. Moreover, low temperature and dry air seem to affect the incidence of several other important respiratory pathogens but not HRV or HEV, suggesting that routes of infection other than aerosol may be relevant for these agents.

Competing interests

None declared.

Funding

Region Västra Götaland Research Funds funded this research. Project number: 162681.

Ethical approval

No personal data were analysed in the study and no ethical approval was required according to Swedish regulations.

Acknowledgment

A special thanks to Katarina Lindström Johansson and the staff at the detection unit at the Department of Virology for their technical expertise.

References

[1] WHO, Influensa (Seasonal). http://www.who.int/mediacentre/factsheets/fs211/en/, 2014.
[2] T.A. Reichert, et al., Influenza and the winter increase in mortality in the United States: 1959–1999, Am. J. Epidemiol. 160 (5) (2004) 492–502.
[3] J. Nielsen, et al., Excess mortality related to seasonal influenza and extreme temperatures in Denmark, 1994–2010, BMC Infect. Dis. 11 (2011) 350.
[4] M. Brink, et al., Respiratory support during the influenza A (H1N1) pandemic flu in Sweden, Acta Anaesthesiol. Scand. 56 (8) (2012) 976–986.
[5] A.I. Barreca, J.P. Shimshack, Absolute humidity, temperature, and influenza mortality: 30 years of county-level evidence from the United States, Am. J. Epidemiol. 176 (Suppl. 7) (2012) S114–S122.
[6] J.A. Weigl, et al., Ten years' experience with year-round active surveillance of up to 19 respiratory pathogens in children, Eur. J. Pediatr. 166 (9) (2007) 957–966.
[7] C.S. Khor, et al., Epidemiology and seasonality of respiratory viral infections in hospitalized children in Kuala Lumpur, Malaysia: a retrospective study of 27 years, BMC Pediatr. 12 (2012) 32.
[8] R. Brittain-Long, et al., Seasonal variations of 15 respiratory agents illustrated by the application of a multiplex polymerase chain reaction assay, Scand. J. Infect. Dis. 44 (1) (2012) 9–17.
[9] M. Lipsitch, C. Viboud, Influenza seasonality: lifting the fog, Proc. Natl. Acad. Sci. U. S. A. 106 (10) (2009) 3645–3646.
[10] E. Lofgren, et al., Influenza seasonality: underlying causes and modeling theories, J. Virol. 81 (11) (2007) 5429–5436.
[11] J.J. Cannell, et al., Epidemic influenza and vitamin D, Epidemiol. Infect. 134 (6) (2006) 1129–1140.
[12] S.F. Dowell, Seasonal variation in host susceptibility and cycles of certain infectious diseases, Emerg. Infect. Dis. 7 (3) (2001) 369–374.
[13] J.D.et al. Tamerius, Environmental predictors of seasonal influenza epidemics across temperate and tropical climates, PLoS Pathog. 9 (3) (2013) e1003194.
[14] Y. Tsuchihashi, et al., Environmental factors and seasonal influenza onset in Okayama city, Japan: case-crossover study, Acta Med. Okayama 65 (2) (2011) 97–103.
[15] R.E. Davis, C.E. Rossier, K.B. Enfield, The impact of weather on influenza and pneumonia mortality in New York City, 1975–2002: a retrospective study, PLoS One 7 (3) (2012) e34091.
[16] K.et al. Jaakkola, Decline in temperature and humidity increases the occurrence of influenza in cold climate, Environ. Health 13 (1) (2014) 22.
[17] G.J. Harper, Airborne micro-organisms: survival tests with four viruses, J. Hyg. (Lond.) 59 (1961) 479–486.
[18] J.H. Hemmes, K.C. Winkler, S.M. Kool, Virus survival as a seasonal factor in influenza and polimyelitis, Nature 188 (1960) 430–431.
[19] A.C. Lowen, et al., Influenza virus transmission is dependent on relative humidity and temperature, PLoS Pathog. 3 (10) (2007) 1470–1476.
[20] A.C. Lowen, et al., High temperature (30 °C) blocks aerosol but not contact transmission of influenza virus, J. Virol. 82 (11) (2008) 5650–5652.
[21] F.L. Schaffer, M.E. Soergel, D.C. Straube, Survival of airborne influenza virus: effects of propagating host, relative humidity, and composition of spray fluids, Arch. Virol. 51 (4) (1976) 263–273.
[22] J. Shaman, M. Kohn, Absolute humidity modulates influenza survival, transmission, and seasonality, Proc. Natl. Acad. Sci. U. S. A. 106 (9) (2009) 3243–3248.
[23] M. Shoji, K. Katayama, K. Sano, Absolute humidity as a deterministic factor affecting seasonal influenza epidemics in Japan, Tohoku J. Exp. Med. 224 (4) (2011) 251–256.
[24] J.et al. Shaman, Absolute humidity and the seasonal onset of influenza in the continental United States, PLoS Biol. 8 (2) (2010) e1000316.
[25] P.W. Chan, et al., Seasonal variation in respiratory syncytial virus chest infection in the tropics, Pediatr. Pulmonol. 34 (1) (2002) 47–51.
[26] S.E. Robertson, et al., Respiratory syncytial virus infection: denominator-based studies in Indonesia, Mozambique, Nigeria and South Africa, Bull. World Health Organ. 82 (12) (2004) 914–922.
[27] A.S. Agrawal, et al., Comparative evaluation of real-time PCR and conventional RT-PCR during a 2 year surveillance for influenza and respiratory syncytial virus among children with acute respiratory infections in Kolkata, India, reveals a distinct seasonality of infection, J. Med. Microbiol. 58 (Pt. 12) (2009) 1616–1622.
[28] B.L. Rao, K. Banerjee, Influenza surveillance in Pune, India, 1978–90, Bull. World Health Organ. 71 (2) (1993) 177–181.
[29] N. Pica, N.M. Bouvier, Environmental factors affecting the transmission of respiratory viruses, Curr. Opin. Virol. 2 (1) (2012) 90–95.
[30] T.J. Meerhoff, et al., Variation of respiratory syncytial virus and the relation with meteorological factors in different winter seasons, Pediatr. Infect. Dis. J. 28 (10) (2009) 860–866.
[31] S. Yusuf, et al., The relationship of meteorological conditions to the epidemic activity of respiratory syncytial virus, Epidemiol. Infect. 135 (7) (2007) 1077–1090.
[32] D.E. Noyola, P.B. Mandeville, Effect of climatological factors on respiratory syncytial virus epidemics, Epidemiol. Infect. 136 (10) (2008) 1328–1332.
[33] Y. Wang, et al., Seasonal distribution and epidemiological characteristics of human metapneumovirus infections in pediatric inpatients in Southeast China, Arch. Virol. 158 (2) (2013) 417–424.
[34] L.M. Casanova, et al., Effects of air temperature and relative humidity on coronavirus survival on surfaces, Appl. Environ. Microbiol. 76 (9) (2010) 2712–2717.
[35] E.R. Gaunt, et al., Epidemiology and clinical presentations of the four human coronaviruses 229 E: HKU1, NL63, and OC43 detected over 3 years using a novel multiplex real-time PCR method, J. Clin. Microbiol. 48 (8) (2010) 2940–2947.
[36] F. Rafiefard, Z. Yun, C. Orvell, Epidemiologic characteristics and seasonal distribution of human metapneumovirus infections in five epidemic seasons in Stockholm: Sweden, 2002–2006, J. Med. Virol. 80 (9) (2008) 1631–1638.
[37] R. Brittain-Long, et al., Multiplex real-time PCR for detection of respiratory tract infections, J. Clin. Virol. 41 (1) (2008) 53–56.
[38] M.E. Andersson, S. Olofsson, M. Lindh, Comparison of the FilmArray assay and in-house real-time PCR for detection of respiratory infection, Scand. J. Infect. Dis. 46 (12) (2014) 897–901.
39. W. Yang, L.C. Marr, Dynamics of airborne influenza A viruses indoors and dependence on humidity, PLoS One 6 (6) (2011) e21481.
[40] M. Reyes, et al., Regular pattern of respiratory syncytial virus and rotavirus infections and relation to weather in Stockholm: 1984–1993, Clin. Microbiol. Infect. 3 (6) (1997) 640–646.
[41] R.C. Welliver Sr., Temperature, humidity, and ultraviolet B radiation predict community respiratory syncytial virus activity, Pediatr. Infect. Dis. J. 26 (Suppl. 11) (2007) S29–35.
[42] S.et al. Vandini, Respiratory syncytial virus infection in infants and correlation with meteorological factors and air pollutants, Ital. J. Pediatr. 39 (1) (2013) 1.
[43] J.B. du Prel, et al., Are meteorological parameters associated with acute respiratory tract infections? Clin. Infect. Dis. 49 (6) (2009) 861–868.
[44] B.G. van den Hoogen, et al., Prevalence and clinical symptoms of human metapneumovirus infection in hospitalized patients, J. Infect. Dis. 188 (10) (2003) 1571–1577.
[45] J.S. Kahn, Human metapneumovirus, a newly emerging respiratory virus, Pediatr. Infect. Dis. J. 22 (10) (2003) 923–924.
[46] J.S. Peiris, et al., Children with respiratory disease associated with metapneumovirus in Hong Kong, Emerg. Infect. Dis. 9 (6) (2003) 628–633.
[47] M. Sansone, et al., Rhinovirus infections in western Sweden: a four-year molecular epidemiology study comparing local and globally appearing types, Eur. J. Clin. Microbiol. Infect. Dis. 32 (7) (2013) 947–954.