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Research Article

The Seasonality of Human Coronaviruses and Future Implications for SARS-CoV-2

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Abstract

The seasonality of influenza viruses and endemic human coronaviruses was tracked over an 8-year period (2013-2020) to assess key epidemiologic reduction points in disease incidence for an urban area in the northeast United States. Patients admitted to a pediatric hospital with worsening respiratory symptoms were tested using a multiplex PCR assay from nasopharyngeal swabs. The additive seasonal effects of outdoor temperatures and indoor relative humidity (RH) were evaluated. The 8-year average peak activity of human coronaviruses occurred in the first week of January, when droplet, aerosol, and contact transmission was enabled by the low indoor RH of 20-30%. Previous studies have shown that an increase in RH from 30% to 50% has been associated with markedly reduced viability and transmission of influenza virus and animal coronaviruses. As disease incidence was reduced by 50% in early March, to 75% in early April, to greater than 99% at the end of April, a relationship was observed from colder outdoor temperatures in January with a low indoor RH to a gradual increase in outdoor temperatures in April with an indoor RH up to 50%. As a lipid-bound, enveloped virus with similar size characteristics to endemic human coronaviruses, SARS-CoV-2 should be subject to the same dynamics of reduced viability and transmission with the seasonal increase in indoor relative humidity. Major factors in the reduction of community SARS-CoV-2 can be attributed to vaccination, acquired natural immunity post-infection, indoor mask-wearing, social distancing, and contact tracing. In addition to these factors, the seasonal effect of the transitioning from lower to higher indoor RH with increasing outdoor temperatures could contribute to the future seasonality of SARS-CoV-2

cases. Over the 8-year period of this study, human coronavirus activity displayed a greater than 99% incidence reduction in the months of June through September, and the future implication would be that SARS-Cov-2 may follow a similar pattern.

Keywords: SARS-CoV-2, atmospheric pollution, inflammation, autoimmune, Metropolitan Region, Brazil

1. Introduction

The seasonality of respiratory viruses, such as influenza A and B and endemic human strains of coronaviruses (HKU1, OC43, NL63, 229E), is recognized in temperate regions of the globe, peaking in winter months. As stated by the WHO and CDC, these viruses as well as SARS-CoV-2 are primarily spread by droplet, aerosol, and contact transmission [1, 2]. Studies of influenza viruses and animal coronaviruses have shown that droplet, aerosol and contact transmission and virus viability is enhanced by cold temperatures, less than 5^0C/41^0F, and by low relative humidity (RH) of 20-30% [3, 4, 5]. This lower humidity can be reached indoors during the winter months in northern temperate regions, during December, January, and February, due to the dryness of indoor heating. For example, when the cold outside temperatures from December to February range from 1^0C/34^0F to 5^0C/41^0F and the inside temperature is set to 22^0C/72^0F, the indoor RH can range from 20-30% and often can drop below 10% [6, 7]. Transmission and infection with coronaviruses also are dependent on the infectiousness of the coronavirus variant itself, on prolonged close contact between susceptible and infected individuals (>15 minutes), and on the immune status and co-morbidities of the exposed host. It is well-recognized that strategies for slowing the spread of respiratory viruses include indoor social distancing, wearing masks, receipt of an appropriate vaccination matching the infecting strain, early case identification by testing, isolation of index cases, contact tracing to identify and quarantine close contacts, and compliance with respiratory hygiene etiquettes. The objective of this study was to examine historical seasonal data from the 8 year-period (Dec 2012-Dec 2020) on the incidence of influenza and human coronavirus infections in pediatric patients requiring hospitalization. Key weekly epidemiologic reduction points were recorded to determine the decline and seasonal end points of hospital admissions due to coronavirus infections. In addition, outdoor temperatures and indoor RH were monitored throughout each year to determine the relationship of these environmental factors on the seasonal course of infection of human coronaviruses with implications for SARS-CoV-2.

2. Materials and Methods

Data was analyzed for the 8-year seasonal influenza and human coronavirus period (Dec 2012- Dec 2020) at a pediatric hospital in north Philadelphia, PA, USA, a temperate zone region at 40^0 North Latitude. A multiplex PCR (polymerase chain reaction) assay was used to detect 17 respiratory viruses and 3 bacteria (Respiratory Pathogens Panel, BioFire Diagnostics, bioMerieux, Salt Lake City, UT, USA) from nasopharyngeal swabs obtained from admitted patients with worsening respiratory symptoms. The percent weekly incidence of infection for influenza A, influenza B, and endemic human coronaviruses (HKU1, OC43, NL63, 229E) were determined from the number of admitted positive patients divided by the total number of admitted patients with respiratory symptoms tested. Weekly disease incidence was recorded for each year and trending was assessed

using 4 data points: week of peak activity, and weekly activity reduction points of 50%, 75%, and greater than 99%. Eight-year weekly averages for the analysis points were determined as the mean weekly date and week of the month. Monthly endemic coronavirus activity was recorded for the 8-year period, 2013-2020, to demonstrate virus seasonality based on the average monthly percent positivity rate.

The relationship of outdoor temperature and indoor relative humidity on disease incidence was measured by recording weekly and monthly endemic coronavirus incidence for the 8-year period in comparison to estimated indoor relative humidity (RH) based on a study by Nguyen and colleagues [6]. Weekly data points for each year were recorded as peak activity of infection and reduction points of 50%, 75%, and greater than 99%. Average weekly and monthly outdoor temperatures and outdoor RH for Philadelphia were recorded from historic averages [8]. Values of measured indoor RH obtained by Nguyen and colleagues [6] in the Boston area, 42^0 N Latitude, were considered applicable to Philadelphia at 40^0 N Latitude, both areas representing the metropolitan northeast temperate zone region of the United States. The use of aggregated patient viral incidence data in this study was reviewed and considered to be exempt from human subjects' ethics review by the Institutional Review Board of Drexel University College of Medicine.

3. Results

The 8-year averages for the week of peak viral activity were: first week in February for influenza A, last week in February for influenza B, and first week in January for the endemic strains of human coronaviruses (Table 1). The average decline for these viruses during the 8 seasons was determined at reduction points of 50%, 75%, and > 99%. For influenza A the 50%, 75% and > 99% average reduction points were the second week of March, fourth week of March, and the fourth week of April. For influenza B, there was a lag of 2 weeks for 50% and 75% reduction points to the fourth week of March, and the second week of April. The reduction point of >99% for Influenza B also occurred in the fourth week of April. For the human coronaviruses the 50% and 75% reduction points were the first week of March and the first week of April, which occurred 12 weeks after the peak and was a slower course of decline than for Influenza A or B which occurred 7 weeks after peak activity. However, the >99% average reduction point for human coronaviruses also occurred in the last week of April (Table 1).

Table 1: Peak Incidence and Key Reduction Points of Influenza and Endemic Coronavirus Infections and Corresponding Week of Occurrence and Percent Incidence

Year	Incidence Status	Influenza A Week of & % Incidence	Influenza B Week of & % Incidence	Coronavirus Week of & % Incidence
2020	Peak	2/16/20 – 18.5%	12/22/19 – 19.3%	1/26/20 – 5.0%
	50% Reduction	3/08/20 – 10.4%	2/02/20 – 10.3%	2/09/20 – 2.0%
	75% Reduction	3/22/20 – 0.8%	3/08/20 – 4.6%	3/08/20 – 1.2%
	>99% Reduction	4/05/20 – 0%	4/05/20 – 0%	4/12/20 – 0%

2019	Peak	2/17/19 – 19%	3/03/19 – 1.5%	2/10/19 – 6.2%
	50% Reduction	3/31/19 – 8.7%	3/17/19 – 0.9%	3/31/19 – 3.3%
	75% Reduction	4/14/19 - 5.6%	4/14/19 - 0%	4/07/19 – 1.7%
	>99% Reduction	4/28/19 – 0%	4/14/19 – 0%	4/21/19 – 0%
2018	Peak	2/04/18 – 10.8%	2/04/18 – 9.0%	12/10/17 – 15.8%
	50% Reduction	3/11/18 – 6.0%	4/15/18 – 4.2%	1/07/18 – 7.8%
	75% Reduction	4/15/18 – 2.1%	4/22/18 – 3.3%	1/28/18 – 5.2%
	>99% Reduction	4/22/18 – 0%	4/29/18 - 0%	3/18/18 - 0%
2017	Peak	2/19/17 – 24.3%	3/19/17 - 9.9%	12/11/16 – 5.4%
	50% Reduction	3/05/17 – 11.3%	4/23/17 - 4.5%	4/09/17 – 2.3%
	75% Reduction	3/12/17 – 4.7%	5/07/17 – 1.4%	5/07/17 – 1.4%
	>99% Reduction	4/23/17 – 0%	5/14/17 – 0%	5/21/17 – 0%
2016	Peak	3/06/16 – 20%	4/03/16 – 5.8%	1/31/16 - 7.1%
	50% Reduction	3/27/16 – 10.1%	4/17/16 – 3.8%	3/20/16 - 2.9%
	75% Reduction	4/10/16 – 5.0%	5/01/16 – 1.1%-	4/17/16 – 1.5%
	>99% Reduction	5/15/16 – 0%	5/29/16 – 0%	5/01/16 – 0%
2015	Peak	1/11/15 – 12.8%	2/22/15 -1.4%	12/07/14 – 4.5%
	50% Reduction	2/15/15 – 4.3%	3/29/15 – 0.7%	2/22/15 – 2.1%
	75% Reduction	2/22/15 – 3.5%	4/05/15 – 0%	4/19/15 - 1.1%
	>99% Reduction	4/05/15 – 0%	4/05/15 - 0%	5/10/15 - 0%
2014	Peak	1/26/14 – 33%	3/30/14 - 6.6%	1/19/14 – 9.6%
	50% Reduction	4/06/14 - 9.8%	4/27/14 – 3.6%	3/16/14 - 5.7%
	75% Reduction	4/20/14 – 5.7%	5/04/14 – 1.8%%	4/14/14 – 2.8%
	>99% Reduction	6/15/14 – 0%	5/11/14 – 0%	5/11/14 - 0%
2013	Peak	1/06/13 - 22.6%	2/10/13 – 16.6%	1/20/13 – 4.7%
	50% Reduction	1/27/13 – 7.3%	3/10/13 – 6.8%	2/27/13 – 2.4%
	75% Reduction	2/03/13 – 5.2%	3/31/13 – 3.8%	4/13/13 – 1.9%

	>99% Reduction	3/10/13 – 0%	4/21/13 – 0%	4/21/13 – 0%
	8-Year Average	**Influenza A**	**Influenza B**	**Coronaviruses**
	Peak Activity	2/05 (1st wk of Feb)	2/24 (4th wk of Feb)	1/09 (1st wk of Jan)
	50% Reduction	3/09 (2nd wk of Mar)	3/28 (4th wk of Mar)	3/04 (1st wk of Mar)
	75% Reduction	3/25 (4th wk of Mar)	4/15 (2nd wk of Apr)	4/14 (2nd wk of Apr)
	>99% Reduction	4/25 (4th wk of Apr)	4/27 (4th wk of Apr)	4/26 (4th wk of Apr)

The seasonality of endemic coronaviruses activity was examined on a local level, by comparing the percent decline of infection to the outdoor temperature in Philadelphia over the 8-year period, 2013-2020 (Table 2) and summarized with reference to indoor RH (Tables 2, 3). The average monthly outdoor RH ranged from 59% to 68% and no correlation was observed between viral activity and outdoor RH (Table 3). At the peak weekly average activity for coronaviruses in the first week of January, the average weekly outdoor temperature was 2^0C/36^0F and the accompanying indoor RH was 20-30% (Table 2).

Table 2: Percent Decline of Endemic Coronaviruses in Relation to Average Weekly Outdoor Temperature and Indoor Relative Humidity in Philadelphia

Year	**Incidence Status**	**Coronaviruses Week of & % Incidence**	**Aver Weekly Outdoor Temperature[a]**
2020	Peak	1/26/20 – 5.0%	10^0C/50^0F
	50% Reduction	2/09/20 – 2.0%	9^0C/48^0F
	75% Reduction	3/08/20 – 1.2%	20^0C/68^0F
	>99% Reduction	4/12/20 – 0%	14^0C/58^0F
2019	Peak	2/10/19 – 6.2%	3^0C/38^0F
	50% Reduction	3/31/19 – 3.3%	9^0C/49^0F
	75% Reduction	4/07/19 – 1.7%	16^0C/61^0F
	>99% Reduction	4/21/19 – 0%	17^0C/63^0F
2018	Peak	12/10/17 – 15.8%	0^0C/32^0F
	50% Reduction	1/07/18 – 7.8%	3^0C/37^0F
	75% Reduction	1/28/18 – 5.2%	2^0C/35^0F
	>99% Reduction	3/25/18 - 0%	8^0C/47^0F
2017	Peak	12/11/16 – 5.4%	1^0C/34^0F

	50% Reduction	4/09/17 – 2.3%	17^0C/62^0F
	75% Reduction	5/07/17 – 1.4%	13^0C/55^0F
	>99% Reduction	5/21/17 – 0%	18^0C/64^0F
2016	Peak	1/31/16 - 7.1%	7^0C/45^0F
	50% Reduction	3/20/16 - 2.9%	11^0C/52^0F
	75% Reduction	4/17/16 – 1.5%	17^0C/63^0F
	>99% Reduction	5/01/16 – 0%	13^0C/55^0F
2015	Peak	12/07/14 – 4.5%	3^0C/38^0F
	50% Reduction	2/22/15 – 2.1%	-3^0C/27^0F
	75% Reduction	4/19/15 – 1.1%	12^0C/54^0F
	>99% Reduction	5/10/15 – 0%	21^0C/70^0F
2014	Peak	1/19/14 – 9.6%	-5^0C/23^0F
	50% Reduction	3/16/14 - 5.7%	6^0C/42^0F
	75% Reduction	4/14/14 – 2.8%	13^0C/55^0F
	>99% Reduction	5/11/14 - 0%	20^0C/68^0F
2013	Peak	1/20/13 – 4.7%	-3^0C/26^0F
	50% Reduction	2/27/13 – 2.4%	4^0C/40^0F
	75% Reduction	4/13/13 – 1.9%	15^0C/59^0F
	>99% Reduction	4/21/13 – 0%	12^0C/54^0F
	Activity Based on 8 –Year Average[b]	**Average Week of Coronavirus Activity**	**Aver Outdoor Temp and Indoor RH[b]**
	Peak Activity	1st week of Jan	2^0C/36^0F – 20-30%
	50% Reduction	1st week of Mar	7^0C/45^0F – 35-40%
	75% Reduction	2nd week of Apr	13^0C/56^0F – 35-45%
	>99% Reduction	4th week of Apr	16^0C/60^0F – 40-50%

a) www.timeanddate.com/weather/usa/philadelphia/historic (8)

b) Estimated indoor RH based on data from Nguyen, JL, et al.(6)

At a 50% incidence reduction point in the first week of March, the average outdoor temperature was 7^0C/45^0F and the estimated indoor RH was 35-40% (Table 2). At a 75% incidence reduction point in the second week of April the average outdoor temperature was 13^0C/56^0F with an estimated indoor RH of 35-45% (Table 2). When the epidemiologic curve for coronaviruses decreased by greater than

99% in the last week of April, the average weekly outdoor temperature was 16^0C/60^0F and the indoor relative humidity had increased to 40-50% (Table 2). Seasonal coronavirus activity, as measured by monthly percent positive cases, showed a relationship from high viral activity with indoor RH in the 20-35% range for the months of December to February, to very low viral activity with indoor RH in the 45-65% range for the months of May to September (Table 3). The initial seasonal increase in human coronavirus activity was detected in the month of October for the 8-year study, which corresponded to indoor RH periodically dropping below the 50% level (Table 3).

Table 3: Monthly Endemic Coronavirus Activity: 8-Year Average Percent Positivity Rate in Relation to Average Monthly Outdoor Temperature and Outdoor Relative Humidity and Estimated Indoor Relative Humidity

Month of Coronavirus Activity	**Monthly Percent Positive (based on 8-yr average from 2013-2020)**	**8-year Total Positive Cases/ Cases Tested**	**Average Outdoor Temperature and Outdoor Relative Humidity[a]**	**Estimated Indoor Relative Humidity[b]**
September	V Low Activity (0.6%)[c]	9/1,636	21^0C/70^0F – 68%	50-65%
October	Low Activity (1.3%)	27/2,013	14^0C/58^0F – 67%	45-60%
November	Mod Activity (2.1%)	63/3,033	9^0C/48^0F – 65%	40-55%
December	**High Activity (3.2%)**	194/6,002	4^0C/39^0F – 65%	**30-40%**
January	**High Activity (3.2%)**	282/8,949	1^0C/34^0F – 65%	**20-30%**
February	**High Activity (2.9%)**	223/7,646	2^0C/35^0F – 61%	**25-35%**
March	Mod Activity (2.6%)	166/6,376	7^0C/44^0F – 59%	35-45%
April	Low Activity (1.3%)	49/3,676	12^0C/54^0F – 59%	35-50%
May	V Low Activity (0.9%)	24/2,677	18^0C/64^0F – 63%	45-60%
June	V Low Activity (0.6%)	14/2,450	23^0C/74^0F – 64%	45-60%
July	V Low Activity (0.8%)	10/1,271	26^0C/79^0F – 64%	50-60%
August	V Low Activity (0.7%)	9/1,258	25^0C/77^0F – 66%	50-65%

a. www.timeanddate.com/weather/usa/philadelphia/historic (8)

b. Estimated indoor RH based on data from Nguyen, JL, et al.(6)

c. Very Low Activity: monthly viral activity less than 1% positive

4. Discussion

In northern temperate regions of the globe, the incidence of respiratory enveloped viruses, such as influenza and endemic human coronaviruses peak in winter months from December to February due to droplet, aerosol, and contact transmission, with added risk factors such as the increase in indoor social crowding and the added effect of low indoor relative humidity (RH). The decline of hospitalized patients admitted with human coronavirus infections, as recorded in Philadelphia, occurs in the months of March and April with an average decline of 75%

occurring in early April and a decline of greater than 99% by the last week of April. One factor contributing to the percent decline of influenza viruses and coronaviruses is the transition from a low indoor RH (20-35%) in winter months to an increase in indoor RH in March and April (35-50%) along with more outdoor exposure and the probable increase in social distancing. Monitoring changes in indoor RH is a key factor related to seasonal virus transmission, and it has been estimated that people in temperate zone metropolitan areas spend more than 90% of their time indoors [10]. A study survey showed that 75% of homes and apartments in a temperate zone do not have humidifiers for winter months to maintain safe indoor RH at 30-50% [6]. Indoor RH should not go above 60% because allergies and other respiratory problems may occur due to mold growth [7]. In this study, increasing indoor RH from 30% to 50% from the winter to spring months corresponded with decreasing viral activity for both influenza and human coronaviruses. In the months of November to March, indoor RH is significantly lower and does not correlate with outdoor RH (Table 3). Indoor RH becomes more aligned with outdoor RH in the months of May to September with the decreased use and stopping of indoor heating in northern temperate regions [6].

A RH of 50% has been shown to have a detrimental effect on the dynamics of droplet and aerosol transmission and virus stability of influenza virus [3, 4]. In a study of animal coronaviruses, which were used as a model for SARS-CoV 2003, the greatest level of virus inactivation also was observed at 50% RH [5]. When a person coughs, sneezes, or talks, the viral particle size can range from 1–100 μm [11]. Under drier conditions, such as 20-35% RH, the evaporation rate of the droplet occurs quickly, and the size of the particle rapidly shrinks to below 5-10 μm [3, 4]. At this small size the droplets can remain airborne for longer periods and many can transform into aerosols (<5 μm particle size), increasing the time and distance over which transmission can occur. The rapid evaporation in dry air causes the NaCl concentrations within the droplet to crystallize out of solution quickly, maintaining virus stability [4]. As the RH increases from 30% to 50%, the droplets evaporate more slowly and their larger size, 20-100 μm, causes them to settle out of the air rapidly. The slower evaporation process causes an increase in the concentration of NaCl within the droplet, resulting in increased osmotic pressure causing inactivation of an enveloped virus [3, 4]. For example, in a study using influenza A virus spiked into mucus droplets, an increased RH from 48% to 52% resulted in a 10-fold reduction in virus viability [4]. When the RH was increased to 70% in the same study, an additional 1 log decrease in viability was noted [4]. The relationship of influenza virus transmission and temperature/humidity also has been demonstrated using a guinea pig model showing that transmission proceeded more rapidly under cold, dry conditions [3]. In contrast, under physiologic conditions as seen in the human respiratory tract with a RH of 99-100%, the NaCl concentrations remain at stationary levels and maintain the viability of influenza viruses. The original Wuhan strain of SARS CoV-2 causing COVID-19 had a higher estimated infectivity rate of R_0 2 – 2.5 compared to influenza virus of R_0 1.6 – 2 [12]. However, the average size (125 nm) of SARS-CoV-2 and overall composition of this virus particle is similar to human endemic coronaviruses (120-160 nm) examined in this study and the effects of humidity should apply to both types of enveloped (lipid-membrane bound) viruses.

The relationship of high seasonal winter activity of influenza and low humidity was demonstrated in a global study of temperate regions of the world with latitudes greater than 25^0 N/S of the equator (13). The study also showed that when tropical countries within 10^0 N/S latitude of the equator experienced their rainy season, their relative humidity was very high at 99-100%, and this corresponded to a higher influenza seasonal activity. These observations are consistent with a humidity range of 50-80% being detrimental to enveloped viruses and a very high humidity of 99-100% being protective of enveloped viruses, such as influenza. In additional, a temperature of 30^0C/86^0F has been reported to be detrimental to influenza virus, which is attained in summer months in northern hemisphere temperate regions [3].

During 2020 and 2021, there were sequential introductions of SARS-CoV-2 strains/variants into different geographical locations in the United States. The epidemiologic transmission and viral surges of SARS-CoV-2 were affected by the indoor air-drying conditions of both heat and air-conditioning and have been different from the monthly transmission patterns of known seasonal human coronaviruses. SARS-CoV-2, a novel coronavirus, was believed to have been initially introduced into areas of the U.S. in Washington state, California, and New York City metropolitan areas in the February-March 2020 time frame, past the annual peak activity of endemic human coronaviruses. However, the laws of physics regarding droplet and aerosol transmission and viability should apply to similar viruses, and the increasing indoor RH from 30% to 50% could have been a contributing factor to the lower transmission during the summer months of 2020. It should be noted that outbreaks of COVID-19 occurred in March 2020 in southern cities with higher outdoor temperatures, such as Miami and New Orleans. These outbreaks most likely were due to close contact transmission (droplet and aerosol) that coincided with Spring Break and Mardi Gras with social indoor crowding and air-conditioning. As physical distancing continued through April and May 2020, the number of hospital admissions for COVID-19 in these areas decreased, as they did in Philadelphia [9]. The added effect of exposure to increasing outdoor temperatures, and the alignment of increasing indoor RH with outdoor RH going into the end of May and into June continued to have a detrimental effect on coronaviruses viability. The transmission of coronaviruses outdoors is highly unlikely, due to air currents diluting any droplet or aerosol transmission, sunlight (UV radiation), and the added effect of outdoor levels of RH that are above 50% throughout the year (Table 3).

Not only does environmental increased humidity slow down respiratory viruses, the beneficial effect of humidity in the nasopharynx helps the innate immune response of the patient [3, 14]. Since humans had not seen SARS-CoV-2 prior to the Fall of 2019, there was no acquired immunity from memory T and B cells until after infection in 2020 in the U.S, and until after the introduction of the vaccines in December 2020. A contributing factor in preventing the progression of infection from the upper to lower respiratory tract in both vaccinated and unvaccinated individuals was the innate immune response of mucociliary clearance. As humidity and temperatures increase, mucus secretions increase in the nasopharynx, along with mucociliary clearance, phagocytosis of viruses by innate immune cells, and the activity of proteases against enveloped viruses [3]. Mucus in the nasal passages facilitates the trapping of viruses and reduces the opportunity for

viral adherence to target cells. One role of the ciliated epithelial cells in the nasopharynx is to remove viruses and bacteria, and these cells can be compromised by years of chemical damage, such as by smoking and exposure to air pollutants. Previous studies have shown that nasal mucociliary clearance is slower when breathing dry air [15, 16]. The use of a humidifier, especially when sleeping at night, would add moisture to the air and help to improve mucociliary clearance. The ideal indoor relative humidity to protect health is considered to be between 30 and 50% [6]. During the day, staying hydrated by periodically drinking water and warm liquids could help to increase nasal secretions. These actions could be helpful, along with the approved vaccines and antiviral therapies. Other approaches such as practicing stress reduction techniques to boost immunity could be helpful, along with taking outside walks on warm humid days (while maintaining distancing) will have a dual effect of breathing fresh, more humid air, and having exposure to sunlight, which is antiviral and boosts natural levels of Vitamin D, helping the immune system.

In tracking human coronaviruses for the past 8 years, a seasonal pattern of decreased viral activity along with increasing indoor RH has been observed in the month of April in Philadelphia, PA, USA, a northeast city at 40^0 North Latitude. In only three of eight years of tracking human coronaviruses did the greater than 99% reductions of activity continue through the middle of May, but in no years did it continue into June. Over the 8-year period, the average monthly human coronavirus activity was very low, below 1%, in the months of May through September, and the implication would be that SARS-CoV-2 would follow a similar pattern. There is always the possibility of the introduction of a new more infectious SARS-CoV-2 variant with immune escape (e.g., Omicron) at any time of the year or local clusters of SARS-CoV-2 infections occurring as sporadic outbreaks throughout the year. The unfortunate timing of the introduction of the more infectious Omicron variant in December 2021 at a time when indoor RH also supported higher viral transmission resulted in the highest SARS-CoV-2 surge to date of the COVID-19 pandemic. As with seasonal endemic coronaviruses, there is a reasonable possibility that SARS-CoV-2 strains will decrease in summer months in northern temperate regions on an annual basis and begin to increase in mid- to late October with the related cooler outdoor temperatures, use of indoor heating, and sporadic reduction in indoor RH below 50%, and cases will peak in the months of December, January, and February.

A limitation of this study was that the percent incidence of seasonal coronavirus infection was based on pediatric hospital admissions. However, hospital admissions are representative of a smaller percentage of infections that are present in the community.

5. Conclusion

Major factors in reducing the sequential epidemiologic surges for SARS-CoV-2, the viral agent of COVID-19, have been acquired natural immunity post-infection, vaccinations, wearing masks, and indoor social distancing. Other contributing factors in reducing the rates of transmission have been adequate case testing and isolation of positive cases, and exposure testing and quarantining. In addition, the patient's innate and acquired immune response plays a major role in reducing the serious outcomes of infection. In addition to social distancing, the exposure to

increased outdoor temperatures together with increased indoor RH should have an additive effect on decreasing the incidence of SARS-CoV-2 during the months of May to September, thus following a seasonal endemic pattern of occurrence. As a lipid-bound, enveloped virus, SARS-CoV-2 is similar in size to endemic human coronaviruses and should be subject to similar dynamics of reduced droplet and aerosol transmission and reduced virus viability as the indoor RH increases from 30% to 50%. Over the 8-year period of this study, human coronavirus activity was less than 1% in the months of May through September, and the implication would be that SARS-Cov-2 would follow a similar pattern.

Ethics Statement

The use of aggregated patient viral incidence data in this study was reviewed and considered to be exempt from human subjects' ethics review by the Institutional Review Board of Drexel University College of Medicine.

Conflict of Interest

The authors have no conflicts of interest for this study

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