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The relationship of meteorological conditions to the epidemic activity of respiratory syncytial virus

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SUMMARY

Our aim was to obtain knowledge of how meteorological conditions affect community epidemics of respiratory syncytial virus (RSV) infection. To this end we recorded year-round RSV activity in nine cities that differ markedly in geographic location and climate. We correlated local weather conditions with weekly or monthly RSV cases. We reviewed similar reports from other areas varying in climate. Weekly RSV activity was related to temperature in a bimodal fashion, with peaks of activity at temperatures above 24–30 °C and at 2–6 °C. RSV activity was also greatest at 45–65% relative humidity. RSV activity was inversely related to UVB radiance at three sites where this could be tested. At sites with persistently warm temperatures and high humidity, RSV activity was continuous throughout the year, peaking in summer and early autumn. In temperate climates, RSV activity was maximal during winter, correlating with lower temperatures. In areas where temperatures remained colder throughout the year, RSV activity again became nearly continuous. Community activity of RSV is substantial when both ambient temperatures and absolute humidity are very high, perhaps reflecting greater stability of RSV in aerosols. Transmission of RSV in cooler climates is inversely related to temperature possibly as a result of increased stability of the virus in secretions in the colder environment. UVB radiation may inactivate virus in the environment, or influence susceptibility to RSV by altering host resistance.

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INTRODUCTION

Respiratory syncytial virus (RSV) is the most important viral respiratory pathogen of early life [1]. Infection by this agent hospitalizes more than 120 000 infants annually in the United States alone [2], and also may be linked to the development of childhood asthma [3]. Our knowledge of how epidemics of RSV are initiated and sustained is incomplete. In geographic regions with temperate climates, epidemics of RSV have been reported to peak during winter in both the Northern and Southern Hemispheres [4, 5]. This suggests that cold weather may increase RSV activity. In contrast, RSV activity has been described as being continuous throughout the year in warm equatorial areas [6, 7], suggesting that temperature cannot be the only factor influencing activity of the virus.

A better understanding of the epidemiology of RSV activity is of more than just intellectual interest. The only effective medical means of preventing RSV infection involves passive prophylaxis with neutralizing antibodies to the virus [8, 9]. Many regions of the world are not served by laboratories that can conduct local virological surveillance. Therefore, other means of predicting the period of the RSV activity must be available if passive prophylaxis is to be used optimally. More importantly, better knowledge of when to institute cohorting of infants with respiratory illnesses in hospitals might be useful in limiting hospital spread of RSV.

We undertook this study to gain a better understanding of the duration of RSV activity in geographic areas that differ widely in climate, and to determine which meteorological conditions might affect the activity of RSV in the community.

METHODS

Determination of community RSV activity

Data on local RSV activity were obtained with the valued cooperation of scientists at each site listed in Table 1. These individuals reviewed laboratory logbooks to provide data on the total number of samples obtained for identification of respiratory viruses, and the percent and absolute number of samples that were positive for RSV. The periods during which surveillance for RSV was maintained and the total number of samples tested for RSV at each site are detailed in Table 1. RSV totals in the six larger cities listed were obtained during routine, year-round surveillance programmes to identify respiratory viruses in general. Data obtained from the Yukon–Kuskokwim Delta area (population 25 000) near Bethel, Alaska, from Mexico City, and neighbourhoods of Delhi, India, were a combination of ongoing year-round surveillance and the special efforts of local physicians interested in RSV epidemiology. At all sites, the same efforts to collect samples were maintained year-round throughout the periods studied. Weekly averages of RSV activity were calculated from data provided by Miami, Houston, Tucson, Buffalo, Winnipeg, and Bethel, while monthly totals were available from Mexico City, Delhi and Santiago, Chile.

Commercial antigen detection methods were used at all sites to identify RSV cases. Individuals at the nine sites identified cases of RSV infection using four different kits, each with sensitivity and specificity of $>90\%$. More importantly, cases of RSV infection initially identified by antigen detection assays were confirmed by culture throughout all years of the study in Miami, Houston, and Winnipeg, and in some study years, in Buffalo, Bethel and Delhi.

Meteorological data for study sites

Data concerning mean temperatures, dew point, relative humidity, precipitation, and barometric pressure were obtained from the nine cities listed in Tables 2 and 3. These sites were chosen to reflect a variety of climatic conditions: warm and wet (Miami, Mexico City, Delhi and Houston), warm and dry (Tucson), cold and wet (Buffalo) or cold and dry (Winnipeg and Bethel). Santiago was chosen as a site from the Southern Hemisphere with intermediate weather conditions. Of the conditions studied, mean daily temperature is self-explanatory. 'Dew point' (the temperature to which a sample of air must be cooled to achieve 100% humidity) is used by weather services to represent the absolute amount of water vapour in the air at a given time (that is, absolute humidity). Absolute humidity is usually reported as 'dew point' (a temperature) because of this indirect, simpler method of determining absolute humidity, and these two terms may be used interchangeably. Absolute humidity is a reflection of new sources of water entering the environment (evaporation, precipitation, etc.) 'Relative humidity' refers to the actual amount of water vapour in the air divided by the maximum amount of water that could be contained in air at that temperature, and is reported as a

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Table 1. *Details of surveillance for respiratory syncytial virus activity*

Site	Duration of surveillance (years)	Dates surveyed	Number of samples obtained
Miami, FL	4	Jan. 2000–Dec. 2003	34–259 per week (median = 123)
Houston, TX	4	Jan. 1999–Dec. 2002*	8–304 per week (median = 63)
Tucson, AZ	4	Dec. 1999–Nov. 2003	6–75 per week (median = 25)
Buffalo, NY	5	Sept. 1995–Aug. 1996, Sept. 1997–Aug. 1999, Sept. 2000–August 2002	10–154 per week (median = 42)
Winnipeg, Manitoba, Canada	2·3	Jan. 2002–Mar. 2004	Unavailable
Yukon–Kuskokwim Delta, Bethel, AK	8	Jan. 1994–Dec. 2000, Jan. 2003–Dec. 2003	1–26 per week (median = 5)
Mexico City, Mexico	2	Jan. 2001–Dec. 2002	12–53 per month (median = 28)
Delhi, India	2	Feb. 2002–Jan. 2004	3–80 per month (median = 30)
Santiago, Chile	5	Jan. 1999–Dec. 2003	4–132 per month (median = 31)

* April 1999 omitted at Houston.

Table 2. *Latitude and climate of selected cities*

City	Latitude	Temperature (mean) (°C)	Dew point (mean) (°C)	Relative humidity (mean %)	Precipitation (mean mm/week)	Range of mean monthly temp. (°C)	UVB radiance (mean W/m² per nm)
Mexico City, Mexico	19·2° N	22·5	6·3	52·4	16·3	13–19	n.a.
Miami, FL	25·8° N	24·2	19·1	56·7	18·0	20–28	124
Delhi, India	28·4° N	23·9	13·9	52	13·5	14–33	n.a.
Houston, TX	29·6° N	20·4	15	49·5	13·0	10–28	n.a.
Tucson, AZ	32·1° N	20·2	1·9	19·3	2·5	11–30	n.a.
Santiago, Chile	33·2° S	14·4	7·8	66	0·3	8–21	n.a.
Buffalo, NY	42·6° N	8·9	3·2	54	9·7	−4 to 22	30·5
Winnipeg, Manitoba, Canada	49·5° N	1·4	−3·8	71·5	0·5	−17 to 20	28·6
Bethel, AK	60·5° N	−1·6	−3·8	n.a.	0·4	−13 to 13	7·1

n.a., Not available.

percentage of that maximum capacity. Relative humidity is therefore altered by rapid changes in air temperature even if no change in the absolute amount of water in the air occurs. Relative humidity may therefore remain elevated even when absolute humidity is low, as long as the simultaneous temperature is also low. Precipitation (rain or snow) and barometric pressure are more easily understood.

Weather conditions simultaneous with periods of RSV surveillance were obtained for all sites listed in Tables 2 and 3. This information was obtained by primary investigators at each site from local weather services, or from the following Internet websites: National Climatic Data Center (www.ncdc.noaa.gov) or WeatherNetwork.com (www.theweathernetwork.com). Data on UVB radiation were also obtained from a website (uvb.nrel.colostate.edu). Data on UVB radiances were obtained using the Langley-calibrated channel, measuring direct surface UVB radiance of 305·5 nM (data were most consistently available for this wavelength). Data on UVB radiance were only available from four of our study sites during the time that this study was performed. UVB data were actually obtained from monitoring sites within 50 miles of the cities included in this study. Weather data for Delhi were obtained from www.worldclimate.com, www.weatherbase.com, or www.crh.noaa.gov. In addition to the original data

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Table 3. *Correlation of meteorological factors with RSV activity in selected cities*

City	Temperature	Dew point	Relative humidity (%)	Precipitation (mm/week)	UVB radiance (W/m²/nm)
Mexico City	0·109	0·409**	0·301**	−0·057	
Miami	0·458*	0·259*	0·22**	0·312*	−0·407*
Delhi	−0·394	−0·508**	−0·195	−0·49	
Houston	−0·39*	−0·389*	−0·016	−0·043	
Tucson	−0·481*	−0·301*	0·18	−0·1	
Santiago	−0·541*	−0·425	0·507**	0·032	
Buffalo	−0·651*	−0·651*	−0·071	−0·022	−0·293**
Winnipeg	−0·338*	−0·351*	0·183	−0·02	−0·290**
Bethel	−0·399**	−0·48**	unavailable	−0·085	0·009

* $P<0·0001$.
** $P \leqslant 0·001$.

generated for this study, we also reviewed published data on the interaction of climate and RSV activity at the additional sites listed in Table 4. These additional sites were chosen because they provided data from latitudes beyond those represented by sites in the present study, or from different hemispheres.

Statistical analysis

Statistical analysis was completed with the assistance of a professional biostatistician (S.S.). The relationship of meteorological conditions to the number of RSV cases identified was determined using a set of confirmatory regressions and correlational approaches. General Linear Methods were used initially, and results were subsequently confirmed using General Additive Measures because of the possibility of autocorrelation. Stepwise and Poisson regressions were conducted independently to determine the relative contribution of meteorological conditions analysed simultaneously. All results were mutually confirmatory for the two approaches. For simplicity of interpretation, only the stepwise regression coefficients are shown in the tables and figures. All statistical evaluations were carried out using SPSS version 12.0 (SPSS Inc., Chicago, IL, USA), and SAS software (SAS Institute, Cary, NC, USA) for confirmatory purposes. Analyses conducted focused on confirmation of correlations, including both parametric and non-parametric techniques used as appropriate based on the nature of distributions. All continuous variables were confirmed to be normally distributed, or to have skewness not significantly different from zero.

Because of the large number of correlations evaluated, only those with probability values of <0·001 were interpreted as significant. We chose to present data on RSV activity as the absolute number of cases ('RSV totals' or 'RSV cases'), since the percentage of isolates positive for RSV could be unduly influenced by the collection of smaller numbers of samples. However, data on the percentage of positive specimens were also obtained.

RESULTS

Meteorological features of selected cities

A summary of meteorological features of the cities from which data were available is presented in Table 2. Weekly averages of the various factors are displayed, except as noted. The meteorological data suggest a reasonable range of temperature, humidity and precipitation among these cities.

RSV activity analysed by latitude

Weekly totals of RSV activity for the six North American sites and are illustrated in Figure 1. In Miami (25·8° N), over the 4-year period of observation, the average peak of RSV activity occurred from weeks 38 to 42 (late September into October, Fig. 1, lower panel). A smaller secondary peak occurred during January and February. RSV activity was continuous throughout all years studied. At least five cases of RSV were identified (and confirmed by culture) during each week of the survey.

In Houston (29·6° N), the peak of RSV activity occurred from mid-October into early January

Table 4. *Correlation of meteorological conditions with respiratory syncytial virus (RSV) activity at individual sites*

Site factor	Correlation coefficient*	Fraction of RSV activity attributable to factor†
Miami, FL		
Mean temperature	0·458	0·21
UVB radiance	−0·407	0·13
Houston, TX		
Mean temperature	−0·39	0·152
Pressure	−0·441	0·042
Tucson, AZ		
Maximum relative humidity	−0·481	0·231
Pressure	0·500	0·019
Buffalo, NY		
Mean temperature	−0·547	0·299
Dew point	−0·562	0·016
UVB radiance	−0·293	0·05
Winnipeg, Manitoba, Canada		
Dew point	−0·345	0·119
UVB radiance	−0·290	0·006
Bethel, AK		
Dew point	−0·439	0·192
Mexico City, Mexico		
Dew point	−0·642	0·412
Delhi, India		
Pressure	0·472	0·223
Santiago, Chile		
Mean temperature	−0·588	0·346

* All probabilities are $<0{\cdot}001$.

† Values confirmed from stepwise regression, confirmed by Poisson regression.

(Fig. 1). RSV was detected (and confirmed by culture) at a rate of 1–4 cases per week during May–August of the first year studied, but was not detected from May–August in years 2 and 3 of surveillance. Thus the autumn peak observed in Miami was diminished or delayed into the winter peak, and RSV activity was less during the summer months.

In Tucson (32·1° N), the peak of RSV activity occurred from January to March (Fig. 1). For each year studied, no cases were identified from late April into late November of most years. Thus there was a further reduction in autumn activity of RSV, no summer activity, and epidemics were focused in the winter months.

In Buffalo (42·6° N), the peak of RSV activity occurred from late December to late April (Fig. 1). From 0 to 5 cases per week were noted in May, early June and late November. RSV was absent from the community from late June to early November. Thus in this cooler climate, winter RSV peaks were of broader duration than in warmer climates, but RSV was also absent during summer and early autumn.

In Winnipeg (49·5° N) and Bethel (60·5° N), the pattern of RSV activity surprisingly became more continuous again (Fig. 1). In Winnipeg, peaks of RSV activity were very broad, extending from December to May. Also, in one of the two summers studied, from 1 to 6 cases of RSV (confirmed by culture) were identified during each week. In Bethel, considerable RSV activity was present from October to May, and cases (confirmed by culture in three of the surveillance years) were frequently identified in summer months.

To attempt to substantiate the relationship of RSV activity to latitude, information was also obtained

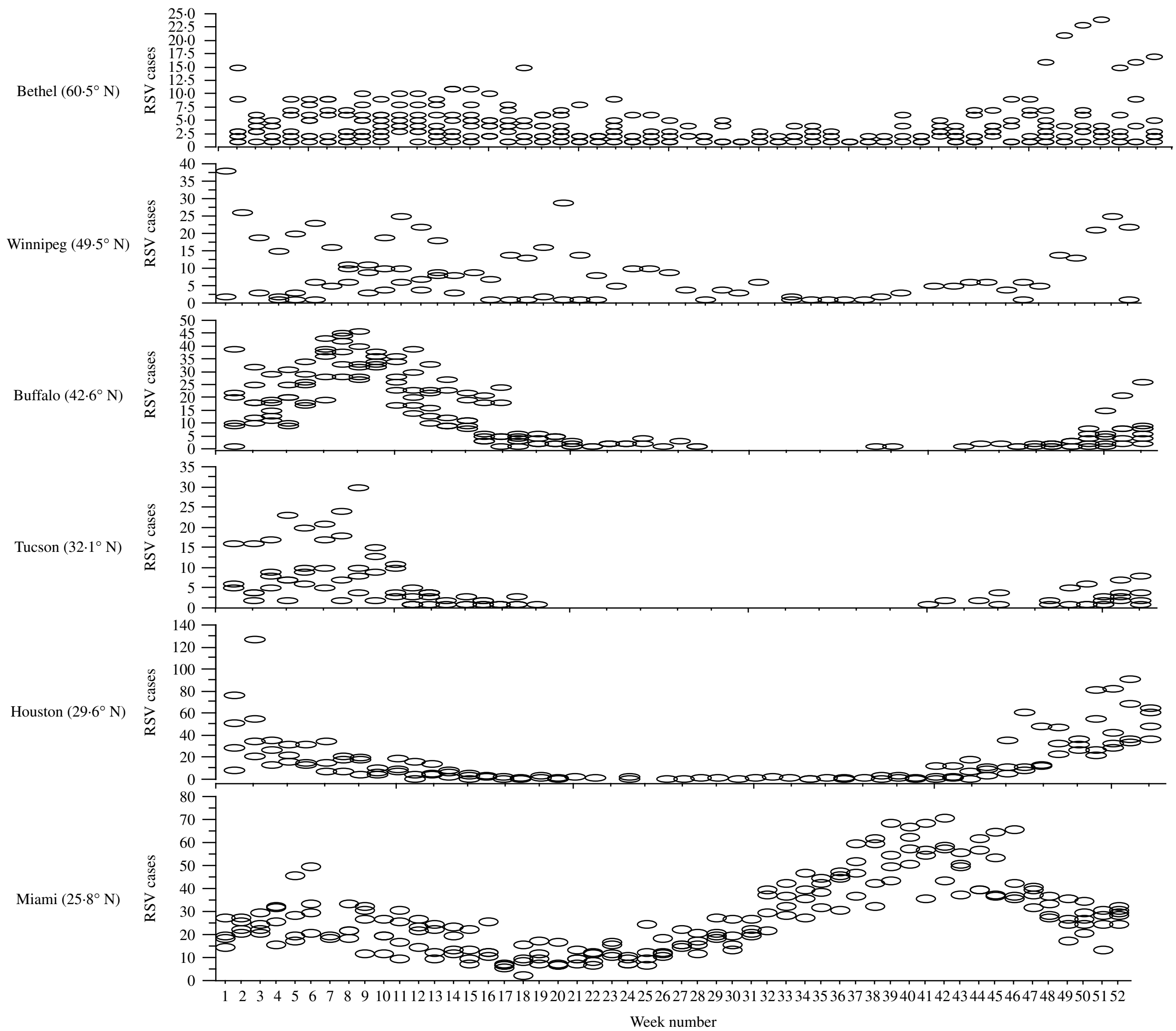

Fig. 1. Total number of respiratory syncytial virus (RSV) cases identified throughout several years of observation in six North American cities. The horizontal axis represents weeks 1–52 for five cities, and months 1–12 for Bethel, AK (only monthly RSV totals were available from Bethel). The vertical axis displays the number of RSV cases identified during each year of surveillance at each site. Each circle represents the total number of RSV cases identified in each week (or, in the case of Bethel, each month) for each year surveyed.

from Mexico City (19·2° N), Delhi, India (28·4° N, or approximately the same distance from the equator as Houston) and Santiago, Chile (33·2° S, or approximately the same distance from the equator as Tucson). In Mexico City, cases of RSV infection were detected in each month of the year (Fig. 2, lower panel), with the greatest number of cases identified in September and October. This pattern of activity is somewhat similar to that observed in Miami. RSV activity in Delhi (Fig. 2, middle panel) was present throughout 10 months of the year (being absent only in the summer months of July and August), with the greatest number of cases in late autumn and winter. Thus the pattern could be interpreted as being similar to that of Houston.

RSV activity in Santiago, Chile, is illustrated in Figure 2, upper panel. A distinct peak of activity was observed in the winter months of July and August. RSV was undetectable from the community during the summer months of December–April in three of the four years studied. Three or fewer cases of RSV were identified throughout the entire months of April and December in the fourth year studied. This pattern might be considered similar to that occurring in Tucson, given the reversal of seasons in these two cities.

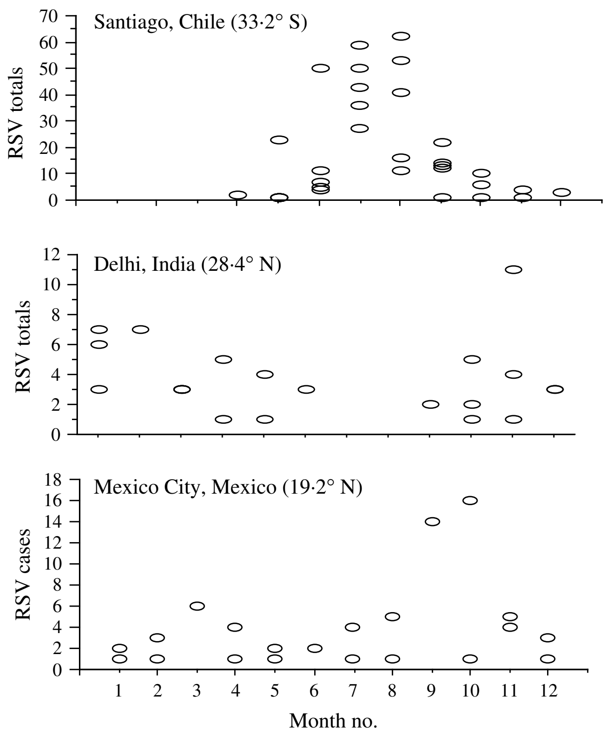

Fig. 2. Total number of respiratory syncytial virus (RSV) cases identified throughout several years of surveillance in Mexico City, Delhi, India, and Santiago, Chile. The horizontal axis represents months 1–12 for each site (only monthly RSV totals were available). The vertical axis displays the number of RSV cases identified during each year of surveillance at each site. Each circle represents the total number of RSV cases identified in each month of each year surveyed.

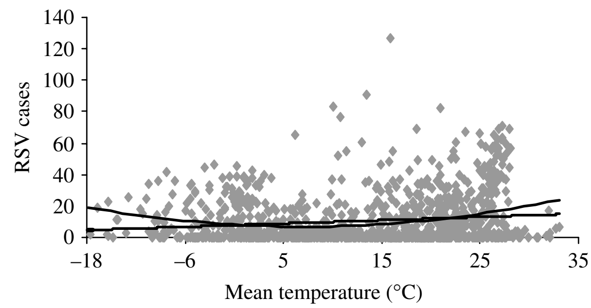

Fig. 3. Relationship of mean temperature to respiratory syncytial virus (RSV) activity in five North American cities. The vertical axis reflects the number of RSV cases identified each week during each year of surveillance at the five study sites that provided weekly RSV totals. The horizontal axis represents the weekly average of mean daily temperatures recorded at intervals corresponding to those for which RSV totals were available. Both linear and curvilinear correlations were calculated (linear $r=0{\cdot}135$, $P=0{\cdot}036$; curvilinear $r=0{\cdot}218$, $P=0{\cdot}021$).

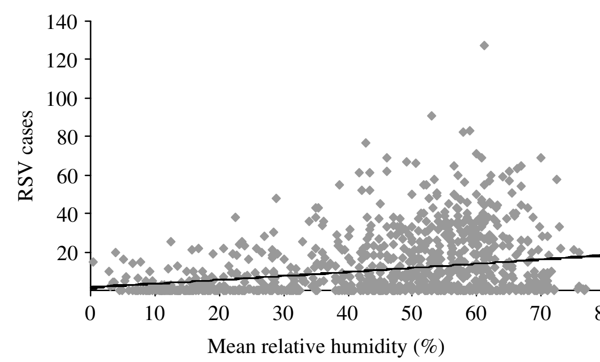

Fig. 4. Relationship of relative humidity to respiratory syncytial virus (RSV) activity in five North American cities. The vertical axis reflects the number of RSV cases identified each week during each year of surveillance at the five study sites that provided weekly RSV totals. The horizontal axis represents the weekly average of mean daily relative humidity (percent) recorded at intervals corresponding to those for which RSV totals were available ($r=0{\cdot}24$, $P=0{\cdot}11$).

While data describing the degree of RSV activity (as expressed by the percent of all samples obtained that were positive for RSV) with season is not illustrated, nevertheless the overall correlation of total RSV cases with the percent of samples positive was quite strong ($r=0{\cdot}874$, $P<0{\cdot}0001$).

Meteorological features and RSV activity

Data for all sites providing weekly data

The association of RSV activity with mean temperature is illustrated in Figure 3. Only those data obtained on a weekly basis were included. A bimodal relationship of RSV activity with temperature was observed. The number of RSV cases increased when the mean temperature was above 24–30 °C, and again when the temperature was in the range of 2–6 °C. Probably because of this bimodal relationship, the relationship of temperature to RSV totals at these sites was not strong (linear $r=0{\cdot}135$, $P=0{\cdot}036$; curvilinear $r=0{\cdot}218$, $P=0{\cdot}021$).

The association of RSV activity and relative humidity is illustrated in Figure 4. RSV activity was increased when the mean relative humidity was between 45% and 65%. The linear correlation was weak ($r=0{\cdot}24$, $P=0{\cdot}011$). UVB radiance was inversely related to the number of RSV cases ($r=-0{\cdot}382$, $P<0{\cdot}001$). No other meteorological factor bore a significant relationship to RSV totals when the sites were analysed together.

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Data for individual study sites

The association of various meteorological features with RSV activity in different locations (based on weekly or monthly data) is summarized in Table 3. The strongest association observed was that of mean temperature and RSV activity, with most correlations having an absolute degree of correlation of $\geqslant 0{\cdot}39$ ($P<0{\cdot}001$). This suggests that RSV activity is dependent on temperature. However, the relationship between temperature and RSV activity is direct in Miami (and, to an extent, in Mexico City), and inverse at all other sites.

We compared RSV activity in the warmest and coldest RSV seasons during the period of study at each site. The degree of RSV activity during these comparatively warm and cold seasons did not differ significantly. The most striking differences were observed in Buffalo, where the mean temperature during the two coldest seasons was $-3{\cdot}7 \pm 0{\cdot}8$ °C, and the mean temperature during the warmest four RSV seasons was $0{\cdot}61 \pm 0{\cdot}6$ °C ($P<0{\cdot}0001$). The weekly mean number of RSV cases identified during these two intervals was $27{\cdot}4 \pm 1{\cdot}9$ *vs*. $23{\cdot}4 \pm 1{\cdot}3$ ($P=0{\cdot}079$).

Dew point

Dew point (reflecting absolute humidity) was also associated with RSV activity, and most correlations were highly significant statistically ($P<0{\cdot}001$, Table 3). This suggests an effect of absolute humidity on RSV activity in the community. The relationship of dew point to RSV activity was again direct in Miami and Mexico City, and inverse at all other sites.

UVB radiance

For Buffalo, Winnipeg and Miami, a statistically significant negative correlation (each $P \leqslant 0{\cdot}001$) was verified between RSV cases and UVB radiance. That indicated that as UVB levels fell, the frequency of RSV cases rose. The UVB and RSV data for Alaska, on the other hand, described no statistically significant relationship. Data on UVB radiance were not available from other study sites during the period of this study.

Relative humidity, precipitation, and barometric pressure

The correlation of relative humidity with RSV activity attained statistical significance in Miami, Mexico City and Santiago, in which positive correlations were observed (Table 3). At other sites, statistically insignificant correlations were observed. Barometric pressure was not significantly associated with RSV activity at any site, while precipitation was significantly correlated with RSV activity only in Miami.

Stepwise regression analysis

Results of stepwise regression analysis of meteorological factors with RSV totals for individual sites are demonstrated in Table 4. In this analysis, the major factor correlated with RSV activity was determined at each site, and the proportion of RSV activity attributable to that factor was calculated. For example, in Miami, mean temperature was the meteorological factor most closely associated with the number of RSV cases identified ($r=0{\cdot}458$, all probability values for correlations shown in the table are $<0{\cdot}001$). In the third column, it can be seen that 21% of RSV activity could be related to temperature changes. When UVB radiance is considered with RSV cases (temperature held constant), 13% of RSV activity could be related to UVB radiance. A similar analysis is provided for all study sites.

In this analysis, temperature was the meteorological condition most strongly associated with RSV activity at four sites overall, including three of the five sites from which weekly RSV data were available. Again, the relationship of temperature to RSV cases was positive at the Miami site, and inverse at other sites. Temperature alone accounted for between 15% and 35% of RSV activity at different sites, with additional increases of up to 4% when other factors were added. The effects of UVB radiance were statistically significant at three sites. UVB effects were somewhat less strong than those of temperature or dew point, and accounted for 0–13% of RSV activity. Either relative or absolute humidity was the principal correlate of RSV cases at four sites (all inverse correlations), accounting for 12–41% of RSV activity. Barometric pressure was the principal correlate of RSV totals at the Delhi site, and a secondary correlate at two others, being related to as much as 22% of total RSV activity.

Because temperature and UVB radiance were interrelated, we repeated the analysis of the contribution of UVB radiance to RSV cases with temperature not held constant (data not shown in tables). By this type of analysis, UVB radiance accounted for 17% of RSV activity in Miami, 8·6% in Buffalo, 8·4% in Winnipeg and 0·9% in Alaska. Precipitation would

Table 5. *Respiratory syncytial virus (RSV) activity, latitude, temperature, and precipitation in previous reports*

Site	Ref.	Latitude	Range of mean monthly temperatures (°C)	Pattern of precipitation	RSV activity
Singapore	[6]	1° N	26–28	Rainy, monsoons Nov.–Jan.	Continuous, with Mar.–Aug. peak
Malaysia	[7]	1° N	26–27	Rainy, monsoons Oct.–Dec.	Essentially continuous, with variable peak
The Gambia, West Africa	[30]	6° N	22–24	Rainy, peak from Apr.–Sept.	Essentially continuous, with Aug.–Oct. peak
Vellore, India	[21]	12° N	29–39	Rain July–Nov., virtually none otherwise	Aug.–Oct. peak, absent otherwise
Hong Kong, China	[26]	22° N	16–29	Rainy, monsoons May–Sept.	Almost continuous, Aug.–Oct. peak
Dhaka, Bangladesh	[27]	24° N	18–29	Very rainy May–Sept., more dry in winter	Almost continuous, peaks in Jan.–April and Aug.–Oct.
Riyadh, Saudi Arabia	[31]	24° N	14–35	Desert. Light rain Nov.–Jan.	Dec–January peak, absent Mar.–Aug.
Kuwait City, Kuwait	[32]	29° N	13–38	Desert. Light rain Nov.-Jan.	Dec.–January peak, absent Apr.–Aug.
Jacksonville, FL	[24]	30° N	11–28	Rainy, peak July–Sept.	Continuous, with Dec.–Feb. peak
Albuquerque, NM	[33]	35° N	1–26	Fairly dry, peak June–Oct.	Jan.–Apr., otherwise absent
Chapel Hill, NC	[4]	35·2° N	4–26	Rainy, slight peak May–Aug.	Jan.–Mar. peak, absent July–Oct.
Oslo, Norway	[34]	59·5° N	−3–16	Heavy precipitation, peak July–Oct.	Nov.–Jan. peak, rare cases throughout summer months

also be expected to correlate negatively with UVB radiance. In this study, however, the correlation of UVB radiance with RSV activity was stronger than that of precipitation with RSV activity at the three sites with substantial UVB radiance (neither UVB radiance nor precipitation correlated well with RSV activity in Alaska). Therefore, the effect of UVB radiance on RSV activity could not have been strongly affected by precipitation.

Review of published reports

We reviewed several published studies to obtain additional information on RSV activity, latitude, temperatures and rainfall from various sites not included in our survey. These additional data are summarized in Table 5. At the two sites near the equator (Singapore and Malaysia) where temperatures are very constant and rainfall is generally heavy, RSV activity was continuous throughout the year. Peak activity occurred from March to August in Singapore (for all references, see Table 5, column 2), while no clear seasonal predominance was observed in Malaysia.

Moving slightly northward, the pattern of RSV activity in The Gambia (West Africa, 6° N) and Vellore, India (12° N) was compared. These two sites each have climates that are equally hot as the equatorial areas above, but vary greatly in rainfall (Table 5). RSV activity peaks in late summer and early autumn in each site. However RSV is nearly continuous in The Gambia where rainfall is 13–361 mm/month throughout the year, but disappears entirely in Vellore during January–March when rainfall is frequently 0 mm/month. Thus, RSV activity is sustained in The Gambia where rainfall is more constant, but the advent of drier weather may interrupt RSV activity in Vellore.

RSV activity in Mexico City, Hong Kong, Dhaka (Bangladesh), Riyadh (Saudi Arabia and Miami (all within 19·2°–25·8° N latitude) can be compared The climate in these cities is somewhat less warm than that of the sites described above (Table 5). Average annual rainfall is high in Hong Kong, Dhaka and Miami, and is somewhat variable in Mexico City (13–183 mm/month during most of the year, but only 6–9 mm/month from November–February). In these four cities RSV is usually present throughout the year. Peaks occur in late summer and early autumn in all four cities, but winter peaks also appear in both Dhaka and Miami. In Mexico City, a slight increase in RSV activity occurred in one of the two winters

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studied. In contrast, Riyadh has hot and dry summers, relatively cooler winters and mild winter rainfall. RSV activity is observed in Riyadh only in winter, in association with cooler temperatures and the minimal rainy season. During the dry season in Riyadh, RSV is absent from April to August, and is minimal in other months. Thus, within this latitude, RSV activity appears to be sustained in cities with rainfall of more than 50 mm/month throughout most of the year. RSV activity has in fact been reported to correlate with rainfall in Miami (Table 3), Hong Kong and Riyadh (see Table 5 for references) although the somewhat cooler temperatures in winter in Riyadh could be considered more important than the modest winter rainfall (maximum 25 mm/month) that occurs there. Again, prolonged dry weather may interrupt RSV activity in Riyadh.

RSV activity can be compared in Houston, Jacksonville, Delhi, Kuwait City, Tucson, Santiago and Albuquerque, since all seven cities lie within 29°–35° N or S (Santiago) latitude. Again the cities with greater annual rainfall (Houston, Jacksonville and Delhi) had more prolonged or occasionally continuous RSV seasons. The drier cities of Tucson, Santiago and Albuquerque (with several months of <5 mm/month of rainfall and never more than 42 mm/month at any time) had prolonged summer periods in which RSV was absent from the community. Rainfall was usually greater in summer in these cities. Interestingly, RSV activity peaked in the colder months in all cities (Northern or Southern Hemispheres), when mean temperatures in the coldest months fell to 1–14 °C.

We were able to compare data from cool (Buffalo) and cold (Winnipeg, Oslo and Bethel) cities. RSV activity in all sites peaked in the winter months. In Buffalo (42·5° N), peaks of RSV activity occurred from December to April, with only rare cases in November, May and June, and none from July to October. In Winnipeg, Oslo and Bethel (49·5°–60·5° N) where severely cold weather was more prolonged throughout the year, RSV seasons were even more prolonged, with cases reported in all summer months in most years. Rainfall and total precipitation was greatest during summer months in all four of these cities.

DISCUSSION

Data generated from the present study and the literature review reveal a complex interaction of latitude, temperature, humidity and UVB radiance with RSV activity. In the present study when data from all sites providing weekly data were included for analysis, a bimodal relationship of temperature and RSV activity was observed, with increased activity at mean daily temperatures above 23·9 °C and below 4·5 °C. RSV activity was also greatest when relative humidity was near 40%. The relationship of RSV activity to absolute humidity (dew point) was positive in Mexico City and Miami, and negative at other sites. At three of four sites where data were available, RSV activity was inversely related to UVB radiance. RSV activity was related positively to relative humidity at some sites. Barometric pressure may contribute somewhat to RSV activity in certain locations, while sunlight and weekly precipitation are not as important.

Potentially important keys to understanding the nature of these relationships are present in laboratory studies of the stability of RSV. Although data are limited, RSV is believed to be transmitted by large-particle aerosols and by direct contact with RSV in solutions of human secretions [10]. Rechsteiner & Winkler [11] prepared stable aerosols (average droplet size = 4·9 μm) of RSV in a cylinder. While temperature was held constant at 20·5 °C, the stability of RSV in aerosol form was tested at degrees of humidity varying from 20% to 90%. Within 1 min of being aerosolized, maximal stability of RSV (loss of <0·09–0·22 $\log_{10}$) was obtained at 80–90% humidity. Maximal inactivation of RSV ($\sim$1 $\log_{10}$) in the first minute occurred at low (20–30%) humidity. When aerosols were maintained for periods of 1–61 min, RSV became most stable at 40% humidity.

Another possibly relevant study is that of Hambling [12], who evaluated the stability of RSV in solutions at varying temperatures. At temperatures of 37 °C, 99% inactivation of RSV takes place over 3 days. At 4 °C, the same degree of inactivation requires more than 6 days. While RSV may not stay stable in nature for these intervals because of the effects of drying, nevertheless it would be expected that a fall in environmental temperatures even modestly below room temperature would markedly prolong the stability of RSV in secretions on fomites if reasonable humidity were maintained.

While only speculation is possible at this point, and while numerous factors other than meteorological conditions surely contribute to the spread of RSV in the community, we present the following possible hypothesis to explain the correlation of temperature and humidity with activity of RSV in an open environment. We suggest that, in tropical and subtropical areas (for example Singapore, Malaysia, The Gambia, Miami), high humidity and stable high temperatures enable RSV to be sustained well enough in large-particle aerosols to permit year-round transmission of the virus. Since maximal rainfall and temperature occur in summer months in theses areas the association of RSV with temperature and humidity would be positive (Table 3). However, the appearance of drier weather (such as in Vellore) might be expected to inactivate RSV more rapidly and interfere with aerosol transmission of the virus.

We hypothesize that, in more temperate climates with more variable temperatures and rainfall than in tropical areas, summertime RSV would only be sustainable in areas with very high rainfall and warm temperatures (for example Delhi, Mexico City, Dhaka, Jacksonville, and possibly, Houston). In more arid regions of the temperate zones (Tucson, Santiago, Riyadh, Kuwait City) aerosol transmission of RSV would be terminated by the lower humidity. The appearance of winter epidemics of RSV in these areas might be influenced by the lower winter temperatures that enhance stability of RSV in solutions of human secretions in the environment. While the reduction in winter temperatures appears modest in these sites (mean January temperatures of 1–13 °C), nevertheless the data from Hambling [12] suggest that even these subtle reductions (which in fact are to temperatures considerably below room temperature) could prolong the survival of RSV on environmental surfaces by days. In these dry areas, a combined effect of cooler environmental temperatures [12] and greater stability of RSV in more sustained aerosols at moderate humidity [11] cannot be excluded. We suspect that the effect of cooling of temperatures in winter is a more significant factor, since winter peaks appear at all locations regardless of rainfall. Also, since rainfall in most of these areas is maximal in summer, RSV activity would correlate negatively with absolute humidity (Table 3). The relationship to relative humidity would be less predictable, but a certain degree of relative humidity would be necessary to prevent drying.

For colder climates (Buffalo, Winnipeg, Oslo, and Bethel), we speculate that the prolonged cold temperatures are again more important than the effects of humidity. If temperatures remain below a threshold that enhances RSV stability for most of the year, RSV activity would be more persistent (and an association with temperature might be less apparent). Thus, RSV activity in colder regions would be expected to be greater in the months of both autumn and spring, when ambient temperatures are similar to those in January at lower latitudes. Gradually warmer temperatures should slowly reduce the degree of spread of RSV during the summer. If the degree of precipitation were also greater during the summer, an inverse correlation of RSV activity with humidity would be expected (Table 3).

Finally, RSV activity was inversely related to UVB radiance. The effect of UVB on RSV cases was greater when total UVB radiance was highest (Miami). The relationship of UVB radiance to RSV cases was less strong in Buffalo and Winnipeg, but still statistically significant. No effect of UVB radiance on RSV cases was observed in Alaska, where total UVB radiance is remarkably low. Therefore, our results suggest that UVB radiance may be an additional determinant of RSV activity in geographic regions with adequate surface UVB irradiation. UVB radiance could interfere with the spread of RSV by inactivating the virus in nature. UVB could also indirectly affect RSV activity by stimulating vitamin D metabolism in the host. While a 10-year Medline search revealed no studies of the effects of vitamin D on the outcome of RSV infection, nevertheless there is a considerable amount of published data suggesting a link between vitamin D metabolism and the activity of respiratory viruses in general.

Vitamin D metabolites induce the activity of antimicrobial peptide genes coding for antimicrobial peptides such as cathelicidin and defensins [13–16]. Some of these proteins have direct antiviral activity [17]. There are very few studies of the effect of vitamin D supplementation on viral infections. However, it has been reported that children with vitamin D-deficient rickets have greater numbers of viral respiratory infections [18]. At least one study has suggested that vitamin D supplementation of these children reduces their frequency of respiratory illnesses to that of control children [19]. Finally a current review has summarized data suggesting a link between vitamin D deficiency and epidemic influenza [20].

Our interpretation of the data might be challenged in several respects. First, it has been stated that extreme cold or very high rainfall might drive populations indoors where RSV would spread more readily [21]. Indoor spread would be independent of external temperature and humidity and would, therefore, reduce the observed statistical association with these climatic factors. Also human susceptibility to viral infection might be altered by weather conditions [6]. These factors undoubtedly account for a great deal of RSV activity, probably more than climate, since only 15–40% of RSV totals could be attributed statistically to meteorological factors. For instance, reopening of schools may contribute to late summer and autumn increases in RSV activity in hot, wet climates where RSV is active during summer. On the other hand, the data in the present study were derived from cities in temperate climates. The mild weather extremes occurring in these cities do not cause substantial changes in human behaviour, yet the effects of temperature and humidity were still statistically significant. Thus, the effects of climate seem to add to the effects of alterations in human behaviour. Alternatively, it is possible that changes in climate might not influence transmission of RSV in nature, but rather activate RSV replication from a latent state in humans.

A second challenge might occur in the area of accepting the validity of summer outbreaks of RSV activity if only antigen detection tests are used without culture confirmation [22]. Since respiratory illness was less common in the summer months, fewer samples for testing may be obtained in summer seasons, and the possible contributions of rare false-positive antigen detection tests might be enhanced. Nevertheless, peaks of RSV activity were observed in summer in many areas, so the number of samples obtained was not small. In addition, no positive tests for RSV were reported in the months of July–September in Buffalo or Tucson throughout several years of observation, yet the frequency of positive tests for RSV in summer in cities such as Shreveport [23], Jacksonville [24] and Miami (Fig. 1) frequently exceed 10%. The differences in frequencies of positive test results in these five laboratories are unlikely to be explained by technical problems. Most importantly, summer cases of RSV were confirmed by culture in the reported literature cited [6, 7, 21, 25, 26] and in Miami, Houston, Winnipeg and Bethel in the present study. Thus, there can be little doubt about the occurrence of RSV infection in summer in these areas. Our data for Miami supplement the CDC surveillance system for the southeastern USA [27], which excludes Florida.

A third limitation might be that the number of samples tested at the different laboratories differed somewhat, thus possibly influencing the number of RSV cases that could be identified at different sites. Nevertheless, physicians caring for subjects hospitalized for respiratory illness were encouraged to obtain samples for detection of viral pathogens throughout the year. We are therefore reasonably confident that the number of respiratory disease cases locally determined the number of samples obtained at a given laboratory. Differences in recovery rates of RSV were, therefore, probably related to the true nature of the epidemiology of the virus, and not by failure to obtain adequate numbers of samples.

Finally, different antigen-detection techniques (immunofluorescence and enzyme immunoassays) were used at the various study sites, possibly affecting the number of RSV cases identified. Each of these assays have been demonstrated to have sensitivities and specificities of $\geqslant 90\%$ for detection of RSV in comparison to cell culture, and in comparison to each other [28, 29]. These assays have supplanted cell culture as the method of choice for detection of RSV in almost all laboratories. It seems highly unlikely that minor differences in the accuracy of the assays employed could account for the marked differences in RSV epidemiology observed at the various study sites.

In summary, community activity of RSV is substantial in tropical areas when both ambient temperatures and humidity are very high (perhaps as a result of prolonged stability of RSV in aerosols), and again in cooler climates if reasonable humidity is maintained (possibly as a result of better stability in secretions in the environment). Reduced UVB radiation may also enhance survival of RSV in nature. Information regarding the timing of and factors activating RSV epidemics is presumably useful in its own right in terms of understanding the epidemiology of this virus. More importantly from a clinical standpoint, knowing when RSV epidemics will begin and end in a community may assist in administrating passive prophylaxis against RSV in a more cost-effective manner, or at least will be helpful in determining when other methods of controlling RSV should be instituted. While there is no substitute in this regard for data derived from local laboratories that accurately reflect the onset and offset of RSV activity in the community, our data on predicting RSV activity could provide assistance in sites where direct measurement of RSV activity will never be possible. Finally, the observations presented suggest that maintaining in-patient areas (or residences) at 30–40% humidity should provide the most rapid inactivation of RSV in recently generated aerosols. UVB irradiation may also be useful in reducing the survival of RSV in closed spaces.

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DECLARATION OF INTEREST

None.

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