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Absolute Humidity as a Deterministic Factor Affecting Seasonal Influenza Epidemics in Japan

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Influenza epidemics occur periodically during the winter season in temperate areas. Characteristic features of winter include low temperature and low humidity. Humidity is expressed in two different ways: absolute humidity (AH) defined as absolute amount of water in the air, and relative humidity (RH) defined as the relative proportion of water in the air in comparison to the maximum water vapor. There have been many arguments for RH as a determinant factor for influenza epidemics. On the other hand, we have been putting emphasis on AH on the basis of our epidemiological observations. In this context, a recent experimental and theoretical study by other investigators has shown that AH correlates with influenza survival, transmission, and seasonality. Accordingly, we collected meteorological and influenza epidemiological data from 46 prefectures in temperate Japan for 1991-1995 and 1999-2009, and analyzed 2,392 sets of weekly compiled data for each season year by using multiple linear regression analysis, in which the numbers of influenza cases were regarded as a function of AH and RH. We found that the standardized partial regression coefficient for AH was consistently stronger than that for RH with statistical significance. In addition, AH increased and decreased significantly at the time of the epidemic onset and subsidence in seven and twelve out of fourteen influenza seasons, respectively, whereas RH did so in none and two out of fourteen influenza seasons. Thus, we have substantiated our quarter-century-old assertion that AH strongly correlates with the onset and subsidence of influenza epidemics.

Keywords: absolute humidity; epidemics; influenza; Japan; relative humidity
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It has been largely unknown why influenza epidemics occur periodically in temperate areas during the winter season. Several proposed hypotheses include environmental factors such as low temperature and relative humidity (RH), indoor heating, and aerosol transport (Lofgren et al. 2007). Lowen et al. (2007) concluded that influenza virus transmission is dependent on both RH and temperature. In sharp contrast, Sharman and Kohn (2009) concluded that absolute humidity (AH) rather than RH modulates influenza survival, transmission, and seasonality.

Independently, we have been working on the relationship between climate change and influenza epidemics in Japan. We reported that water vapor pressure, or namely AH, rather than RH, was closely related to outbreaks of influenza epidemics over two decades ago (Shoji 1985). On this basis, we invented an algorithm to forecast influenza epidemics in Japan with considerable success (Shoji 1988).

Sharman and Kohn's (2009) conclusion that AH is the single key factor that can explain influenza seasonality was deduced from experimental analyses. In this report, we reanalyzed our previously published data (Shoji and Katayama 2009) to examine whether epidemiological and meteorological data obtained in temperate Japan could substantiate the key role of AH in regulating influenza epidemics.

Materials and Methods

Meteorological data and influenza epidemics

Meteorological data were reported from Japan Meteorological Agency, Tokyo, and AH was calculated from the average temperature and RH. Weekly reports of influenza cases per sentinel in the prefectures of Japan were obtained from Infectious Disease Surveillance Center, Tokyo for the period 1991 to 2010, except for the period 1995 to 1999, during which the surveillance system was changed and data were not available. Each influenza season in this paper spans from the 27th week to the 26th week of the next year. An influenza epidemic at each prefecture was defined as occurring when one or more influenza cases per sentinel were reported for three consecutive weeks. The first week of the three consecutive weeks is defined as

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the week of epidemic onset. An epidemic was defined to be over when the numbers of influenza cases per sentinel was below one.

Statistical Analyses

AH and RH from Japanese prefectures, except semi-tropical Okinawa, were used for the analyses. To quantitatively evaluate the impact of AH and RH on the influenza epidemics, the numbers of influenza cases per sentinel were analyzed as a function of AH and RH using multiple linear regression analysis, as these two variables are independent on the basis of the definition. Before analysis, both AH and RH were standardized to a distribution with a mean of 0 and a standard deviation of 1, so that partial regression coefficients could be used for direct comparison between the two predictor variables. The Student's paired *t*-tests were used to compare AH or RH between before and after the epidemic onset or subsidence.

Results

AH, rather than RH is closely related to influenza epidemics

We have previously published the data of AH and influenza epidemics in Japan (Shoji and katayama 2009). In this paper, we re-examined whether AH or RH was more closely related to influenza epidemics. As one example, the numbers of influenza cases per sentinel were shown in rela-

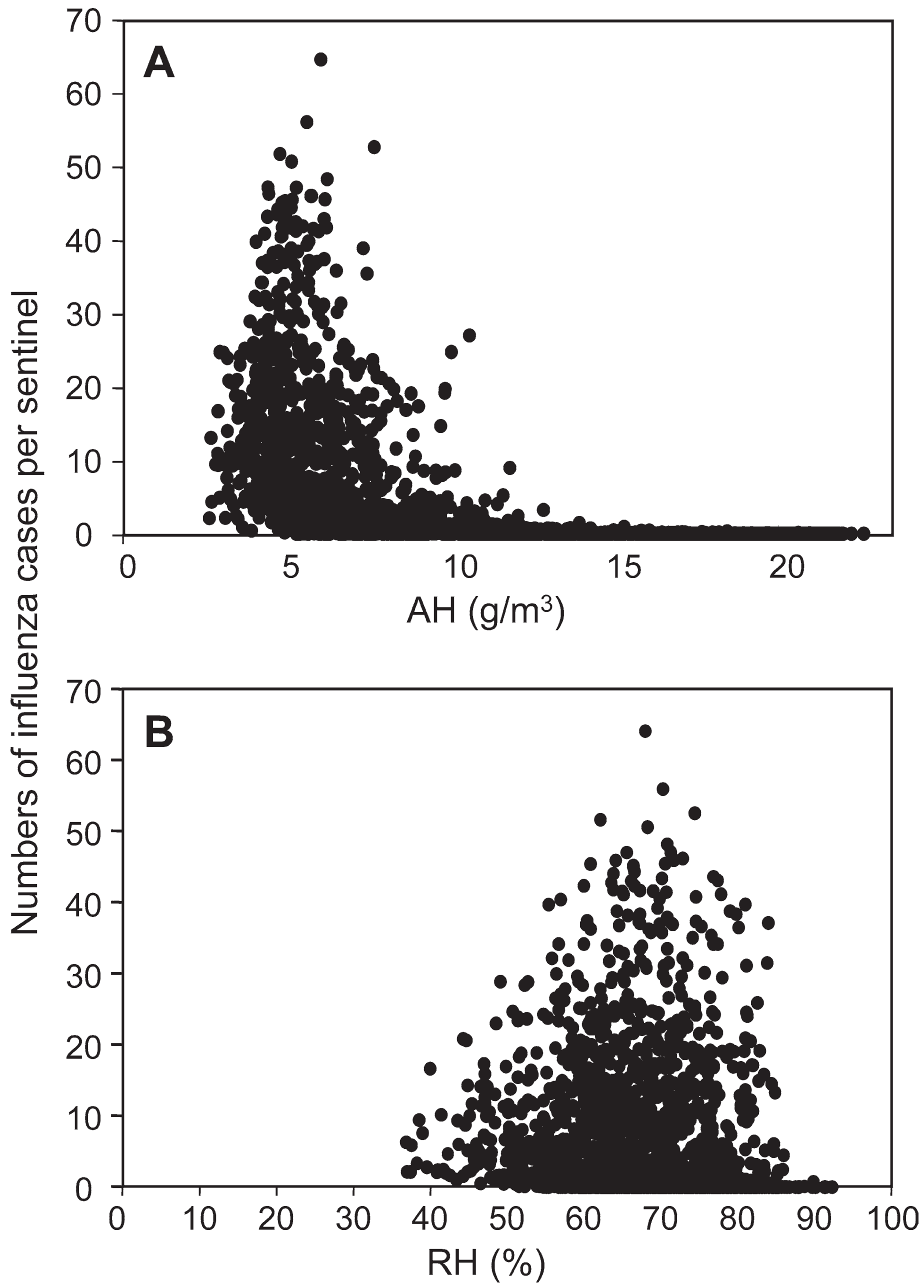

Fig. 1. Close relationship of AH, but not RH, to influenza epidemics in 2008-2009 season year.
The numbers of influenza cases per sentinel are shown in relation to AH (A) or RH (B) in 46 prefectures weekly for the 2008-2009 season (2,392 samples). Influenza epidemics predominantly occurred at low AH (A), but were independent of RH (B).

tion to AH (Fig. 1A) or RH (Fig. 1B) in 46 prefectures weekly for the 2008-2009 season year. The data set of 2,392 samples appeared to show that influenza epidemics predominantly occurred at low AH (Fig. 1A) but independently of RH (Fig. 1B).

To substantiate this phenomenological trend in a quantitative manner, we employed multiple linear regression analysis regarding the numbers of influenza cases per sentinel as a function of AH and RH for each season year (2,392 samples in regular years and 2,438 samples in leap years). In all seasons examined, the standardized partial regression coefficient for AH was consistently stronger than that for RH with statistical significance (Table 1). Thus we conclude that AH is more closely correlated with the influenza epidemics than RH in temperate areas of Japan.

Close correlation of epidemic onset and subsidence with AH, but not RH.

To examine whether the influenza epidemic onset or subsidence is correlated with changes in AH or RH, we compared AH and RH between before and after influenza epidemic onset or subsidence. Data in 2008-2009 are shown as an example in Fig. 2, where 46 samples collected from 46 prefectures in Japan, excluding semi-tropical Okinawa, were plotted in relation to the epidemic onset (Fig. 2A and C) or subsidence (Fig. 2B and D). AH at the week of epidemic onset was significantly lower than that at one week prior to the onset (Fig. 2A). Inversely, AH significantly increased at the week of the epidemic subsidence in comparison to at the preceding week (Fig. 2B). RH did not change after the epidemic onset (Fig. 2C), while RH became higher when the epidemic ended in this season.

Data summed up from 14 influenza seasons running from 1991 to 2010 (46 samples each year) revealed a general trend. In fourteen and twelve out of fourteen influenza seasons, RH did not change when the influenza epidemics started and subsided (Table 2), respectively. In sharp contrast, AH increased and decreased significantly at the time of the epidemic onset and subsidence in seven and twelve out of fourteen influenza seasons, respectively (Table 2). These epidemiological data collectively indicate that AH is more closely related to influenza epidemic than RH.

Discussion

We have been examining the issue of whether AH or RH is more closely related to outbreaks of influenza epidemics. Initially, we found that influenza epidemics were more closely related to the water vapor pressure than RH (Shoji 1985). Recently, Sharman and Kohn (2009) described that AH modulates influenza survival, transmission, and seasonality. The water vapor pressure expresses the amount of water in the air as the partial pressure in hectoPascal, and is synonymous with AH expressing the water vapor as the density in g/m^3. We published our observation (Shoji 1985) similar to but 24 years in advance of that by Sharman and Kohn (2009), and have started forecasting influenza epidemics in Japan with considerable success (Shoji 1988). Since their conclusion was deduced mainly from experimental and theoretical analyses, we support our previous finding by reanalyzing our own data using statistical methods previously not employed for this issue.

We have been emphasizing that influenza epidemics

Table 1. AH rather than RH is closely related to influenza epidemics.

Year	coefficient		*P* value	
	AH	RH	AH	RH
2008 - 2009	−0.569	0.086	4.72×10^{-166}	6.31×10^{-6}
2007 - 2008	−0.538	0.065	2.15×10^{-138}	1.32×10^{-3}
2006 - 2007	−0.305	−0.208	3.30×10^{-44}	5.18×10^{-22}
2005 - 2006	−0.464	0.059	3.60×10^{-96}	5.25×10^{-3}
2004 - 2005	−0.431	−0.011	3.86×10^{-97}	6.10×10^{-1}
2003 - 2004	−0.444	0.025	1.31×10^{-81}	2.60×10^{-1}
2002 - 2003	−0.500	0.049	1.08×10^{-128}	1.18×10^{-2}
2001 - 2002	−0.390	−0.100	3.10×10^{-77}	7.96×10^{-7}
2000 - 2001	−0.296	−0.170	7.53×10^{-44}	6.72×10^{-16}
1999 - 2000	−0.475	0.134	4.97×10^{-90}	3.78×10^{-9}
1994 - 1995	−0.364	−0.065	5.27×10^{-65}	1.78×10^{-3}
1993 - 1994	−0.282	−0.098	1.89×10^{-28}	1.12×10^{-4}
1992 - 1993	−0.412	0.005	1.19×10^{-70}	$8.08 \times 10^{-}1$
1991 - 1992	−0.301	−0.108	2.98×10^{-41}	1.01×10^{-6}

AH, RH and the numbers of influenza cases per sentinel were obtained weekly from 46 prefectures in each year. The data sets consist of 2,392 samples in regular years and 2,438 samples in leap years. The numbers of influenza cases per sentinel were analyzed as a function of standardized AH and RH using multiple linear regression analysis. A stronger partial regression coefficient for AH than for RH in all years examined implies that AH has more profound effects on influenza epidemics than RH does.

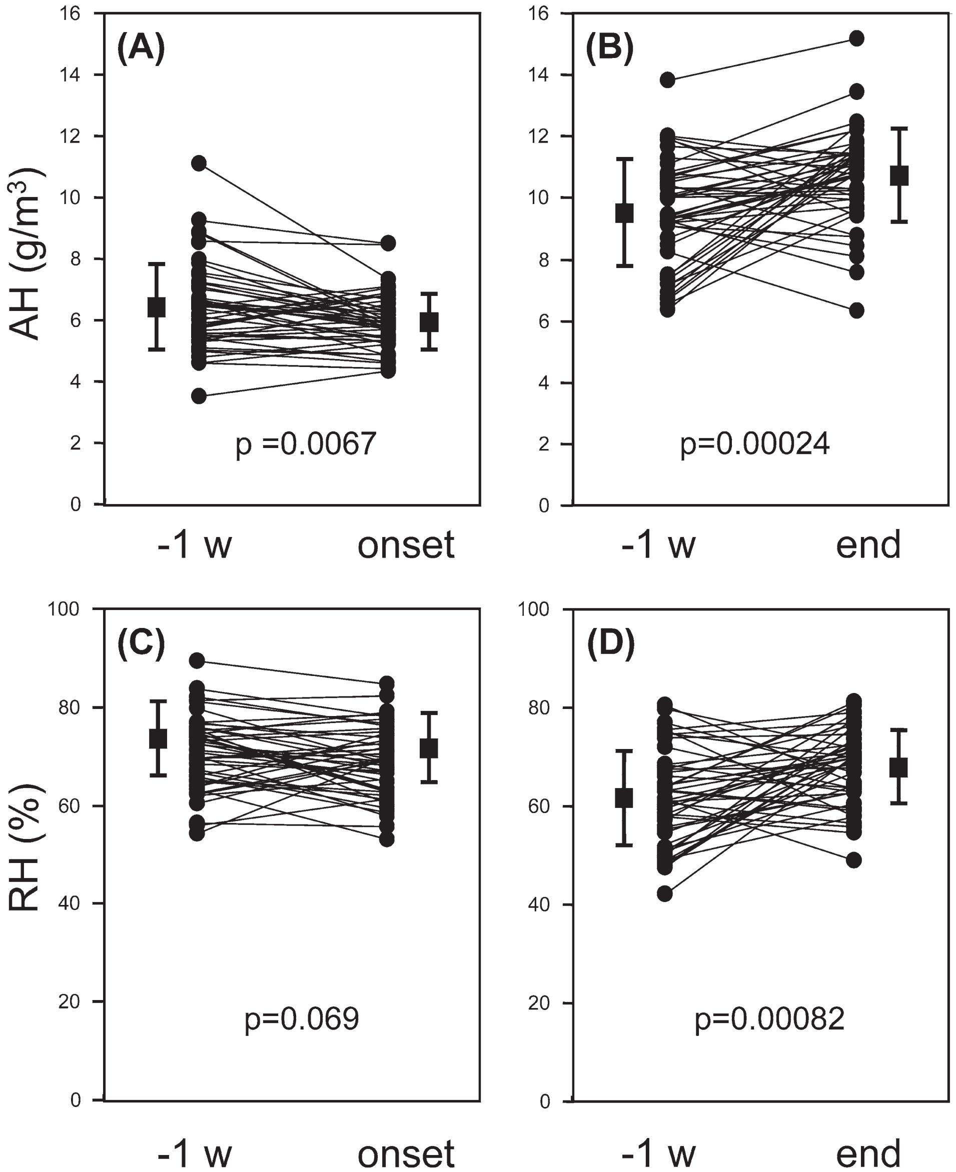

Fig. 2. Changes in AH and RH at the time of epidemic onset and subsidence in 2008-2009.
AH (A, B) and RH (C, D) were compared between at the week of influenza epidemic onset and at the preceding week (−1 w) (A, C) or between at the week of epidemic end and at the preceding week (−1 w) (B, D). Forty-six paired samples shown in each figure correspond to AH or RH at 46 prefectures in temperate Japan during the 2008-2009 season. Column represents the means with the bar as standard deviation. The paired Student's *t* test was used for statistical analysis.

start below 11 g/m^3 of AH on the basis of the epidemiological data that not even a single influenza epidemic ever occurred at or above 11 g/m^3 of AH for the 14 seasons examined (Shoji and Katayama 2009). In this manuscript, we took a closer approach by comparing AH between before and after the epidemic onset, and found that influenza epidemics started at an average of 4.93 g/m^3, in contrast to 5.08 g/m^3 in the preceding week, in temperate regions in Japan (Table 2). This result can be interpreted as meaning that influenza epidemics have occurred in roughly half the areas in Japan when the AH drops down to less than 5 g/m^3. These results could apply forecasting the influenza epidemics in other temperate areas.

Our initial study concerning the correlation between influenza epidemics and vapor pressure, namely AH (Shoji 1985), had been prompted by the report of Harper (1961), who found that the survival of influenza virus was dependent on both the temperature and RH. On that basis, we sensed a closer relationship between influenza survival and AH. Our repeated analyses of actual meteorological data and influenza epidemics substantiated our initial view.

Low temperature would also be a strong driving factor for influenza epidemics. When we used the same statistical analysis for temperature, we could not observe significant dominance of AH over temperature. We are currently developing more sensitive way to weigh AH and tempera-

Table 2. Parallel decrease and increase in AH, but not RH, with epidemic onset and end, respectively.

Year	AH (g/m^3)				RH (%)			
	Onset		end		onset		end	
	−1 w	0 w	−1 w	0 w	−1 w	0 w	−1 w	0 w
2008 - 2009	6.43	5.97*	9.53	10.72*	70.67	68.79	61.64	67.96*
2007 - 2008	6.48	5.88*	6.65	7.01	67.71	67.74	63.24	62.39
2006 - 2007	4.58	5.01	9.87	10.37*	65.39	67.13	63.67	63.16
2005 - 2006	4.45	3.98*	8.66	9.39*	63.21	63.29	63.44	64.60
2004 - 2005	4.31	4.47	9.22	9.81*	66.01	66.60	61.85	63.32
2003 - 2004	5.10	4.56*	5.78	6.43*	65.75	64.74	59.20	60.97
2002 - 2003	5.36	5.43	7.14	7.86*	70.59	70.07	64.52	66.25
2001 - 2002	4.60	4.96	8.60	9.11*	65.41	67.58	64.33	64.30
2000 - 2001	4.18	4.31	8.15	9.09*	67.13	66.84	60.33	64.71*
1999 - 2000	5.06	4.99	4.58	4.97*	66.81	67.05	60.43	59.56
1994 - 1995	5.24	4.87*	6.44	6.83*	68.80	68.31	64.35	62.61
1993 - 1994	4.37	4.33	6.81	7.39*	65.70	64.00	59.46	59.12
1992 - 1993	6.07	5.64*	5.96	6.14	69.47	68.66	62.83	61.54
1991 - 1992	4.83	4.56*	6.27	6.62*	68.60	67.59	72.83	74.40
Mean	5.08	4.93	7.40	7.98	67.23	67.03	63.01	63.92

AH and RH were compared between at the week of influenza epidemic onset and at the preceding week or between at the week of epidemic end and at the preceding week. Shown are mean of 46 samples of AH or RH from 46 prefectures, and statistical analysis was performed using the paired Student's *t*-test. Asterisk indicates that the change in AH or RH was significant ($p < 0.05$) at the indicated year.

ture.

Inverse relationship between indoor and outdoor RH in winter was discussed in the paper by Shaman and Kohn (2009). In contrast to the US, both outdoor and indoor RH as well as AH rise in summer and reversely drop in winter in Japan. The humidity dip would facilitate influenza infection both inside and outside houses in winter.

Sharman et al. (2010) adopted an anomaly analysis to minimize the confounding seasonal effects in their paper. We, however, did not employ a similar analytical method for several reasons. First, we needed to maintain consistency with our previous works in which raw climatological data were analyzed. And we deduced significant difference between AH and RH from analyses of raw data sets even without reducing possible seasonal turbulence in advance. Finally, we are concerned that we might lose track of the essential link between influenza epidemics and climatological changes once we subtract season-related anomalies from climatological data.

In this study, we focused on the 46 prefectures at temperate zone, but not on Okinawa prefecture located in semi-tropical zone. Influenza epidemics in Okinawa prefecture share some features, including year-round prevalence, with those at other tropical regions (Higashiuesato and Yamane 2005). Summer influenza epidemics in Okinawa subside at a surprisingly high level of AH (over 17 g/m^3), in contrast to below 11 g/m^3 in the rest of Japan (Shoji and Katayama 2011). Such differences are partly explained by the hypothesis that longer stays at home in the rainy season facilitate close contact with influenza patients at home (Higashiuesato and Yamane 2005). We reason that a drop in AH owing to the prevalence of air-conditioners prolonged the survival of influenza viruses in the air (Shoji and Katayama 2011). Further empirical confirmation will be needed.

In summary, we provide further evidence for our long-held contention using statistical analyses of meteorological and influenza epidemiological data in temperate Japan. The peculiar features of influenza epidemics in semi-tropical Okinawa need to be analyzed further.

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Conflict of Interest

We have no conflict of interest.

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