Effects of Temperature and Air Pollutants on Cardiovascular and Respiratory Diseases for Males and Females Older than 65 Years of Age in Tokyo, July and August 1980–1995

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We studied exposures to higher daily maximum temperatures and concentrations of air pollutants in Tokyo during the summer months of July and August from 1980 to 1995 and their effects on hospital emergency transports for cardiovascular and respiratory diseases for males and females > 65 years of age. Cardiovascular diseases were angina, cardiac insufficiency, hypertension, and myocardial infarction. Respiratory diseases were asthma, acute and chronic bronchitis, and pneumonia. Except for pneumonia, daily maximum temperatures were not associated with hospital emergency transports. Increasing daily maximum temperatures, however, were associated with decreased hospital emergency transports for hypertension. Concentrations of nitrogen dioxide or particulate matter ≤ 10 µm, however, were associated with daily hospital emergency transports for angina, cardiac insufficiency, myocardial infarction, asthma, acute and chronic bronchitis, and pneumonia. For cardiac insufficiency, hypertension, myocardial infarction, asthma, chronic bronchitis, and pneumonia, the expected daily number of emergency transports per million were greater for males than for females. For angina and acute bronchitis, there were no differences for the expected daily number of emergency transports per million between males and females. Key words: air pollutants, cardiovascular disease, elderly, respiratory disease, temperature. Environ Health Perspect 109:355–359 (2001). [Online 13 March 2001] http://ehpnet1.niehs.nih.gov/docs/2001/109p355-359ye/abstract.html

Previous studies have examined exposures to daily maximum temperatures and air pollutant concentrations during the warm summer months of July and August in Tokyo and their effect on the daily number of hospital emergency transports per million for heat stroke (1) and three cerebral vascular diseases: cerebral hemorrhage, cerebral infarction, and cerebral ischemia (2). Both studies indicated that males and females > 65 years of age had the highest daily number of heat stroke and cerebral vascular disease hospital emergency transports per million of any age group to four Tokyo city hospitals. For heat stroke, exposures to daily maximum temperatures (Tmax) and concentrations of nitrogen dioxide were associated with the daily number of hospital emergency transports per million residents. Exposures to higher Tmax were associated with a decrease in the daily number of hospital emergency transports per million residents for cerebral hemorrhage. For cerebral infarction, hospital emergency transports per million were associated with increasing daily average NO2 concentrations. For cerebral ischemia, exposures to Tmax and daily average ozone concentrations were associated with the daily hospital emergency transports per million residents.

For these four diseases, it was evident that increasing or decreasing numbers of hospital emergency transports per million were not associated with the same set of temperature and air pollutant variables. Therefore, additional studies to examine hospital emergency transports for other diseases as functions of daily maximum temperatures and air pollutant concentrations needed to be conducted on a disease-by-disease basis.

The studies on cardiovascular and respiratory diseases in Tokyo were undertaken because in the next 50–100 years, there could be a doubling of atmospheric concentrations of carbon dioxide (3). This could raise surface temperatures year-round by 1–3°C and result in a greater frequency and longer duration of heat waves during warmer months of the year. In Tokyo but in many other major urban areas worldwide. Also, the number of people > 65 years of age in Tokyo is increasing (4), and this population appears to be most vulnerable to higher temperatures and higher air pollutant concentrations.

The months of July and August in Tokyo are when daily maximum temperatures are the highest and when many air pollutants have high concentrations because of atmospheric chemical and photochemical reactions and meteorological conditions that cause air pollutant concentrations to be high at ground level, especially in large, urban areas. Therefore, months of the year were selected when the frequency of exposures to both higher daily maximum temperatures and air pollutant concentrations would be the greatest.

The covariates that were used to determine if temperature or air quality may be associated with each cardiovascular and respiratory disease were Tmax and air pollutant concentrations for NO2, O3, sulfur dioxide, carbon monoxide, and particles with aerodynamic diameters ≤ 10 µm (PM10). We chose Tmax temperatures over average daily temperatures (Tavg), and minimum daily temperatures (Tmin), because Tmax temperatures represented the maximum levels of heat stress that could occur on a daily basis. Tmax was also selected over the heat index because Tmax can be more directly associated with core body temperatures. The heat index is not a temperature and is calculated from a complex polynomial expression for temperature and relative humidity that makes it difficult to separate the temperature contribution from the relative humidity contribution. The cardiovascular diseases that were examined and their International Classification of Disease, 9th Revision (ICD-9) codes included hypertension (ICD-9 codes 401–405), myocardial infarction (ICD-9 code 410), angina (ICD-9 code 413), and cardiac insufficiency (ICD-9 code 428). The respiratory diseases included acute bronchitis (ICD-9 code 466), pneumonia (ICD-9 code 486), chronic bronchitis (ICD-9 code 491), and asthma (ICD-9 code 493).

There is an extensive literature about the association between daily mortality and hospital admissions for cardiovascular and respiratory diseases and daily changes in air pollutant concentrations and climate variables (5–36). This literature was important in selecting variables that may affect hospital emergency transports in Tokyo. Exposures to air pollutants have been associated with damage to lung tissues and have been shown to have significant effects on pulmonary function (37–42). Because of the interrelationship of the cardiac and pulmonary systems, damage to lung tissue is an important factor not only in many respiratory diseases, but in many cardiovascular diseases as well. In many epidemiology studies with respiratory and cardiovascular diseases, regression models include adjustments for seasonal climate variability to isolate the contributions of air pollution on the daily number of deaths or hospital admissions for these diseases. The...
focus of this study, however, was on the months of July and August. We selected these months to obtain an indication of how prolonged exposures to both higher temperatures and air pollutant concentrations could affect hospital emergency transports for a wide variety of diseases.

Data Characteristics and Model Development

We obtained data on hospital emergency transports to four Tokyo city hospitals for each of the four cardiovascular and respiratory diseases for the summer months of July and August, 1980–1995, for males and females > 65 years of age from the Tokyo Emergency Office. In all cases, if a record of transport had been entered into the data collection system for the Tokyo Emergency Office, the patient was transported by an emergency vehicle to the hospital and admitted for the diagnosed disease. The diagnosis was made by the attending physician in the emergency room and was based on the symptoms that the patient presented at the time of arrival. The daily number of hospital emergency transports per million residents for the four cardiovascular and respiratory diseases were determined from population data provided by the Ministry of Health and Welfare (4). Because information was not available on the percentage of males and females in this age group from 1980 to 1995, we assumed that 50% was male and 50% was female. From 1980 to 1995, the percentage of the population within the city limits of Tokyo of males and females > 65 years of age has increased from 7.7% (894,586) in 1980 to 13.2% (1,553,772) in 1995, even though the total population has remained relatively constant at 11.8 million.

To determine if there were annual trends in the daily number of hospital emergency transports per million for July and August, we calculated the annual daily average number of cardiovascular disease hospital emergency transports per million for each disease for males and females (Figure 1). The data indicated that the annual daily average numbers of angina and cardiac insufficiency hospital emergency transports per million increased for both males and females in July and August from 1980 to 1995, whereas the annual daily average number of hypertension hospital emergency transports per million appeared to decrease for males and females. There did not appear to be much change in the annual daily average number of myocardial infarction hospital emergency transports per million from 1980 to 1995. However, there did appear to be significant differences in response between males and females for all diseases. From these observations, we concluded that classification variables were needed in the regression model for each cardiovascular disease to account for differences between sexes and annual changes in the July and August number of emergency transports per million.

In a similar manner, we calculated the annual daily average number of hospital emergency transports per million for July and August for each respiratory disease (Figure 2). The annual daily average number of pneumonia and asthma hospital emergency transports per million appeared to increase for both males and females from 1980 to 1995. The annual average number of hospital emergency transports per million for acute and chronic bronchitis, however, appeared to be unchanged from 1980 to 1995. There did appear to be significant differences in response between males and females for all diseases. As with the cardiovascular diseases, this behavior indicated that classification variables were needed in the regression models for each respiratory disease to account for differences between sexes and for annual changes in the July and August number of emergency transports per million.

For the daily number of emergency transports for each cardiovascular and respiratory disease for July and August, 1980–1995, calculations of means and variances of their density functions for each disease are given in Table 1. For the most part, these calculations indicated that the density functions for each disease could be assumed to be Poisson distributed. However, the means and variances were not equal for the distributions for cardiac insufficiency, asthma, and pneumonia. As a result, there may be overdispersion in the distributions for all diseases that will need to be evaluated.

We obtained daily average concentrations of air pollutants and climate variables for Tokyo from the Japan Environment Agency. Summary statistics for each of the variables used in this analysis for July and August, 1980–1995 are given in Table 2. Table 3 contains the Pearson correlation coefficients among air-quality variables and Tmax. For the study periods, these results indicate possible correlations between NO₂ and PM₁₀, NO₂ and CO, and PM₁₀ and CO. The daily average concentrations of NO₂ and CO and Tmax temperatures increased slightly during this time, indicating that yearly trends in model covariates would need to be taken into account by model calculations.

Analysis Methods

We fit generalized linear models (GLM) to hospital emergency transport data for each disease to determine which covariates were significantly associated with each of the four cardiovascular and four respiratory diseases (43). A GLM was used because daily numbers of hospital emergency transports per million for each disease were count data. Because only data for emergency transports for July and August were used, confounding
effects from seasonal variability were likely to be minimal. In addition, because only data from July and August were being used in this study, it was assumed that the daily number of hospital emergency transports per million for each disease and the daily data for each covariate within any given year were independent of daily disease count and daily covariate data from previous years.

Within each 2-month period in each year, however, the daily number of hospital emergency transports and the daily maximum temperature and daily average air pollutant concentration data for a given day can be correlated with the data for each of these variables from previous days. To account for autocorrelations in the temperature and air quality variables, we included lag times of 1–4 days for each of these covariates as additional model variables. Generalized estimating equations that accounted for serial correlations in the daily number of emergency transports per million data for each disease were used to estimate values for the coefficients of each model covariate (44). The correlation structure for the covariance matrix of these generalized estimating equations was assumed to be autoregressive. When an exchangeable correlation structure was used, model parameter estimates were nearly the same as those estimates given by the autoregressive structure of the covariance matrix. Based on the data given in Figures 1 and 2, classification variables were also included in the models for each disease to account for sex and for unexpected annual trends in the daily number of hospital emergency transports per million and annual trends in T_{max} and air pollutant concentrations. We used PROC GENMOD from SAS software (45) to model the number of hospital emergency transports per million for each cardiovascular and respiratory disease for males and females for July and August from 1980 to 1995 and to provide parameter estimates for model covariates.

The model for the expected daily number of emergency transports per million for each cardiovascular and respiratory disease (ET) for males and females > 65 years of age is given as

$$\ln(ET) = X\beta,$$

where $X$ is a matrix that includes a column of 1s for the intercept; classification variable columns for sex and for annual trends; columns for the daily values for $T_{max}$ and/or air pollutant variable with lag times of 1–4 days; columns for interaction effects between pairs of model covariates as indicated from the correlation analysis given in Table 3; and $\beta$ is the vector of model coefficients for each model covariate. Population changes from 1980 to 1995 have been included as an offset or normalizing factor in this model so that the expected daily number of hospital emergency transports are expressed as the expected daily number of hospital emergency transports per million. This makes it possible to include changes in population for each 2-month interval from 1980 to 1995.

To determine which covariates were significant for each disease, we constructed an initial series of models for each of the individual covariates and their lag effects. These initial models for each disease also contained classification variables for sex and annual trends. After each round of model fitting, insignificant model variables were eliminated as indicated by their significance probabilities or p-values, and a reduced model was constructed for the next round of calculations. This process was repeated until the most significant model covariates and classification variables for each disease were identified. At this point variables that included interactions between model covariates and covariates and classification variables were added to the model to determine if they were significant. In the final models, the effects of overdispersion in the count data for each disease were negligible.

### Table 1. Cardiovascular and respiratory diseases studied: means and variances of the daily number of hospital emergency transports for males and females > 65 years of age in Tokyo, July–August, 1980–1995.

| Disease (ICD-9 code) | Males Mean | Males Variance | Females Mean | Females Variance |
|----------------------|------------|----------------|--------------|------------------|
| Cardiovascular diseases |            |                |              |                  |
| Angina (413)          | 1.79       | 2.03           | 1.88         | 2.25             |
| Cardiac insufficiency (428) | 2.21 | 2.65           | 2.56         | 3.70             |
| Hypertension (401–405) | 0.96       | 0.97           | 1.54         | 1.61             |
| Myocardial infarction (410) | 1.93 | 2.05           | 1.35         | 1.43             |
| Respiratory diseases  |            |                |              |                  |
| Acute bronchitis (446) | 0.21       | 0.23           | 0.19         | 0.20             |
| Asthma (493)          | 1.28       | 1.59           | 1.16         | 1.41             |
| Chronic bronchitis (491) | 0.11 | 0.12           | 0.07         | 0.07             |
| Pneumonia (486)       | 2.33       | 3.75           | 1.86         | 3.14             |

The population in Tokyo and females > 65 years of age increased from 0.895 million in 1980 to 1.544 million in 1995. The total population remained relatively constant at 11.8 million from 1980 to 1995. About 50% of the population is assumed to be male and 50% is assumed to be female.

### Table 2. Summary statistics for T_{max} and concentrations of NO_{2}, O_{3}, PM\textsubscript{10}, SO_{2}, and CO in Tokyo, July–August, 1980–1995.

| Variable | No. of observations | Minimum | Maximum | Mean (SD) |
|----------|---------------------|---------|---------|-----------|
| T_{max} (°C) | 992 | 17.3 | 36.5 | 28.9 (3.8) |
| NO_{2} (ppb) | 907 | 5.3 | 72.2 | 25.4 (11.4) |
| O_{3} (ppb) | 990 | 0.05 | 59.4 | 13.9 (9.8) |
| PM_{10} (µg/m\textsuperscript{3}) | 902 | 7.3 | 185.4 | 48.0 (27.1) |
| SO_{2} (ppb) | 948 | 0.6 | 28.8 | 7.0 (4.8) |
| CO (ppb) | 972 | 41.7 | 2354.2 | 667.2 (314.9) |

### Table 3. Pearson correlation coefficients for T_{max} and air pollutant variables.

| Variable | T_{max} | NO_{2} | O_{3} | PM_{10} | SO_{2} | CO |
|----------|---------|--------|------|---------|-------|----|
| T_{max}  | 1.000   | 0.021  | 0.313 | 0.122   | 0.078 | 0.066 |
| NO_{2}   | -       | 1.000  | 0.183 | 0.643   | 0.333 | 0.759 |
| O_{3}    | -       | -      | 1.000 | 0.376   | 0.259 | 0.202 |
| PM_{10}  | -       | -      | -    | 1.000   | 0.306 | 0.754 |
| SO_{2}   | -       | -      | -    | -       | 1.000 | 0.389 |
| CO       | -       | -      | -    | -       | -     | 1.000 |
differences for the expected daily numbers of emergency transports per million between males and females. $T_{\text{max}}$ was a significant model covariate only for pneumonia. Concentrations of NO$_2$ were significant model covariates for angina, cardiac insufficiency, myocardial infarction, and acute bronchitis. Concentrations of PM$_{10}$ were significant model covariates for asthma, chronic bronchitis, and pneumonia. For hypertension, the daily expected number of hospital emergency transports per million decreased as daily $T_{\text{max}}$ increased.

Many studies (3, 25, 27–34) have shown correlations between hospital admissions for cardiovascular diseases and CO concentrations. However, the associations between the four cardiovascular diseases and concentrations of CO in these studies for July and August in Tokyo do not appear to be very strong. A possible explanation for this observation may be that daily average concentrations of CO during the study period were 0.67 ppm (SD = 0.31 ppm). Morris et al. (5), in their study of seven U.S. cities, found average year-round mean concentrations 3–9 times higher than those observed in the present study. Because of the lower mean CO concentration in Tokyo, CO appears to have minimal impact on the daily number of hospital emergency transports for the four cardiovascular diseases that were studied.

For this group of cardiovascular and respiratory diseases, even though conditions were chosen so that daily temperatures would be at their maximum values, exposure to concentrations of NO$_2$ and PM$_{10}$ during the summer months of July and August in Tokyo appeared to be much more significant model covariates for many of these diseases than were exposures to daily maximum temperatures. However, $T_{\text{max}}$ was a contributing factor for pneumonia.

It would be incorrect to conclude, however, that higher temperatures that may occur as a result of climate change would not be a significant covariate for many of these diseases. Any time increased cardiac output is required to return core body temperatures to normal ranges and there are people with cardiovascular and respiratory systems that are not functioning at optimal levels because of age or preexisting disease, there is an increased probability of emergency transport for a particular cardiovascular or respiratory disease as daily maximum temperature increases. Future modeling work for these diseases will examine the year-round response to temperature and concentrations of air pollutants and will require the use of generalized additive models (14, 46).

As with the heat stroke and cerebral vascular disease studies, it is important to note that the model covariates were not the same for each disease. This is not a surprising result because the physiologic and molecular mechanisms for each disease are different, even though cardiovascular and respiratory functions are highly interconnected. Even so, the results of this study strongly suggest that each disease should be considered separately rather than grouped together. It should be noted that possible factors that could be confounders in these studies are the smoking habits of this age group of males and females. Smoking habits and the presence of chronic cardiovascular and respiratory diseases, however, should not change from day to day. Therefore, these existing conditions should not be confounding factors in this study (31). Finally, it is well known that hypertension is a precursor for congestive heart failure (cardiac insufficiency in our nomenclature), but it was not possible to account for the possible interrelationships between these two diseases because data on blood pressure at the time of emergency transport and hospital admission for individual patients were not available.

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| Disease | Model covariate* | Coefficient estimate (SE) | 95% Confidence limits | Z-Value* | Pr > |Z|c |
|---------|------------------|----------------------------|-----------------------|----------|-----|-----|
| Cardiovascular diseases | | | | | | |
| Angina | NO$_2$ | 0.007 (0.001) | 0.004 | 0.009 | 4.8 | 0.0000 |
| Cardiac insufficiency | NO$_2$ | 0.006 (0.002) | 0.003 | 0.009 | 3.54 | 0.0004 |
| Hypertension | $T_{\text{max}}$ | -0.152 (0.03) | -0.209 | -0.095 | 5.26 | 0.0000 |
| Mycardial infarction | NO$_2$ | -0.014 (0.005) | -0.02 | -0.004 | 2.8 | 0.0056 |
| NO$_2$ | -0.044 (0.004) | -0.052 | -0.36 | -11.00 | 0.0005 |
| Respiratory diseases | | | | | | |
| Asthma | PM$_{10}$ | 0.003 (0.001) | 0.000 | 0.006 | 3.32 | 0.0009 |
| M | 0.011 (0.03) | 0.006 | 0.017 | 4.1 | 0.0000 |
| Acute bronchitis | NO$_2$ | 0.014 (0.005) | 0.004 | 0.024 | 2.67 | 0.0075 |
| Chronic bronchitis | PM$_{10}$ | 0.006 (0.002) | 0.001 | 0.001 | 2.60 | 0.0102 |
| Pneumonia | PM$_{10}$ | 0.038 (0.007) | 0.012 | 0.065 | 5.24 | 0.0000 |
| | 0.002 (0.001) | 0.000 | 0.005 | 4.3 | 0.0000 |

*$T_{\text{max}}$, PM$_{10}$, and NO$_2$ are the time series for same-day $T_{\text{max}}$ and concentration of PM$_{10}$ and NO$_2$, and PM$_{2.5}$-2 is the time series for PM$_{2.5}$-2 with a 2-day lag time. **Z-values are calculated as the coefficient estimate/SE. *Pr > |Z| is the significance probability.
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