Effects of Air Pollution on Blood Pressure: A Population-Based Approach

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ABSTRACT

Objectives. This analysis assessed the association between blood pressure, meteorology, and air pollution in a random population sample.

Methods. Blood pressure measurements of 2607 men and women aged 25 to 64 years who participated in the Augsburg Monitoring of Trends and Determinants in Cardiovascular Disease survey were analyzed in association with 24-hour mean concentrations of air pollutants.

Results. During the air pollution episode in Europe in January 1985, an association between blood pressure and air pollution was observed, which disappeared after adjustment for meteorology. Continuous concentrations of total suspended particulates and sulfur dioxide were associated with an increase in systolic blood pressure of 1.79 mm Hg (95% confidence interval [CI]=0.63, 2.95) per 90 μg/m^3 total suspended particulates and 0.74 mm Hg (95% CI=0.08, 1.40) per 80 μg/m^3 sulfur dioxide. In subgroups with high plasma viscosity levels and increased heart rates, systolic blood pressure increased by 6.93 mm Hg (95% CI= 4.31, 9.75) and 7.76 mm Hg (95% CI= 5.70, 9.82) in association with total suspended particulates.

Conclusions. The observed increase in systolic blood pressure associated with ambient air pollution could be related to a change in cardiovascular autonomic control. (*Am J Public Health.* 2001;91: 571–577)

Recent studies in Europe and the United States investigated adverse effects of day-to-day variations in outdoor particle concentrations on both mortality and morbidity. Results showed an increase in cardiovascular and respiratory deaths among elderly people as well as increased hospital admissions for heart disease and asthma.[1–12] Several hypotheses regarding causal pathways have been suggested.

Seaton et al.[13] proposed that high particle concentrations, particularly in the ultrafine range, can provoke alveolar inflammation, which might release mediators capable of exacerbating lung disease and increasing blood coagulability in susceptible individuals. It was also hypothesized that particle inhalation induces an inflammatory response in the lungs with a subsequent release of chemical mediators that alter the autonomic nervous system control of cardiac rhythm.[14] A recent study by Godleski et al.[15] showed a disturbance in cardiac rhythm and increases in broncheoalveolar lavage neutrophils in dogs exposed to concentrations of air particles.

The results of a study by Pope et al.[16] indicated an increase in pulse rate in association with ambient particulate matter less than 10 μm in diameter. No association was found between blood oxygen saturation and ambient particulate matter. Analyses of daily variation in particulate air pollution and cardiac autonomic control in elderly people found that increased levels of particulate matter less than 2.5 μm in diameter are associated with lower heart rate variability, pointing at poor cardiac autonomic control.[17] Another recently published study[18] found small but consistent effects of particulate air pollution on heart rate variability. Gold et al.[19] showed that particulate air pollution was associated with altered autonomic function of the heart. These findings could reflect changes in cardiac rhythm, indicating a possible mechanistic link between particulate matter and cardiovascular disease morbidity and mortality.

In January 1985, an air pollution episode occurred throughout central Europe,[20] resulting in an elevated number of hospital admissions for cardiovascular diseases, which were attributed to admissions for acute coronary syndromes and arrhythmia.[21] During this time, the first survey under the World Health Organization's project to MONItor trends in CArdiovascular diseases (MONICA) was carried out in Augsburg, southern Germany.[22] A retrospective analysis of these data showed elevated levels of plasma viscosity in association with total suspended particulates.[23] Furthermore, an increase in heart rate was observed during the air pollution episode compared with nonepisode days.[24]

Several parameters, such as heart rate, heart rate variability, blood oxygen saturation, and plasma viscosity, all known risk factors for cardiovascular mortality and morbidity, have been analyzed in association with air pollution. Effects of air pollution on blood pressure, a well-established risk factor for cardiovascular morbidity and mortality,[25] have not yet been documented. The purpose of this article is to discuss the association between blood pressure, meteorologic parameters, and elevated levels of air pollution during the Augsburg MONICA surveys in 1984–1985 and 1987–1988.

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Methods

Study Area and Population

The study was conducted in the area of Augsburg, which is located in southern Germany in the western part of Bavaria. The study area includes the city of Augsburg and 2 rural districts, the county of Augsburg and the county of Aichach–Friedberg, with a total population of 531 401 in 1981. The city of Augsburg is situated 489 m above sea level, with an area covering 147 km^2. Of this portion, 49 km^2 are farmland, and 37 km^2 are used for forestry.

The first MONICA survey in Augsburg was carried out in 1984–1985 to provide reliable prevalence estimates of cardiovascular risk factors in the study area. A detailed description of the study population and sampling procedures is given in the survey manual.[26] Of the 5069 randomly sampled eligible subjects, aged 25 to 64 years, 4022 took part (response rate = 79.3%).

In 1987–1988, participants of the first MONICA survey were reexamined with the same methodology and protocols as 3 years earlier. Of the 4022 study participants from the first survey, 3753 took part in the 1987–1988 follow-up (93.3%). Loss to follow-up was the result of deaths (46 participants), relocation (9 participants), and refusal to participate (214 people). All survey methods were as described in the MONICA protocol.[26] A uniform age and sex distribution over time was preserved by design for both examinations. Valid blood pressure measurements were available for all 3753 study subjects.

The results reported here are based on a retrospective analysis of a subsample of 2681 men and women, in whom valid electrocardiogram recordings were obtained in both surveys in addition to valid blood pressure measurements. Furthermore, a valid plasma viscosity measurement in the first survey had to be available. There were no major differences in conventional cardiovascular risk factors between the subgroup considered in this article and the total sample.[22,24] For the statistical analyses, only individuals with complete information on physiologic variables, meteorologic data, and air pollution data in both surveys were included (n = 2607).

Physiologic Measurements

Trained medical personnel measured blood pressure with the Hawksley random-zero sphygmomanometer. Three blood pressure measurements were taken according to the standardized conditions of the *MONICA Manual* and in agreement with the American Heart Association.[27] Following a 30-minute rest period, measurements were taken in a seated, upright position at intervals of no less than 3 minutes. During each measurement, the first, fourth, and fifth phase of the Korotkoff sounds and the pulse rate were recorded. Three cuff sizes (bladder size 12×23 cm, 12×28 cm, and 14×40 cm) were used, depending on the circumference of the right upper arm of the study subject.

Interobserver and intraobserver variation were assessed throughout the survey as part of the quality assurance procedures.[28] Mean systolic and mean diastolic blood pressure were calculated, and the second and third measurements were averaged. Hypertension was defined according to the World Health Organization and the International Society of Hypertension criteria: systolic blood pressure of at least 140 mm Hg, diastolic blood pressure of at least 90 mm Hg, or both.[29] The mean heart rate was determined from electrocardiogram records with a duration of 20 seconds by means of computerized electrocardiogram analysis systems that provided consistently operating measurement algorithms for all electrocardiogram records analyzed.[24] Plasma viscosity was tested with blood samples drawn with only short-term venous occlusion and minimal suction. Measurement procedures and sample preparations met the criteria of the International Committee for Standardisation in Haematology and have been described elsewhere.[23]

Air Quality Measurements

Sulfur dioxide, carbon monoxide, and total suspended particulates were measured as part of the automated Bavarian air quality network.[23] The monitoring station was located in the center of the city, whereas temperature, relative humidity, and barometric pressure were measured in the outskirts of the city. Air pollution was considered in 2 ways in the analyses: (1) as an indicator for the 1985 episode and (2) as the continuous concentrations of sulfur dioxide, total suspended particulates, and carbon monoxide. The pollution episode was defined as a period of 3 or more consecutive days with sulfur dioxide concentrations above 150 $\mu g/m^3$. For both surveys, 24-hour mean concentrations of sulfur dioxide, carbon monoxide, and total suspended particulates measured midnight to midnight were available.

Statistical Analysis

We used Gaussian regression models for repeated measures in Proc Mixed in the SAS System (SAS Institute, Inc, Cary, NC) to model the association between systolic blood pressure and air pollution. The procedure allows adjustment for within-subject effects. In accordance with previous analyses,[24] categoric variables were constructed to control for age (10-year categories), current smoking, and cardiovascular medication. Body mass index and total and high-density lipoprotein cholesterol entered the models as continuous variables. Meteorologic parameters were considered as possible confounders in the regression analyses. To model the influence of the meteorologic parameters appropriately, we included in the model linear, quadratic, and indicator variables for temperature, relative humidity, and barometric pressure. We determined model fit by taking into account information on the Akaikes information criterion, *P* value, and change in the effect estimate for the pollutant effect. In the final model, temperature was categorized as below freezing, 0°C to 10°C, and above 10°C; the indicator variable for relative humidity had a value of 1 if relative humidity exceeded 80% and 0 if it was 80% or lower; and barometric pressure was included in the model as a continuous variable.

Effect estimates were calculated for episode days vs nonepisode days, and the indicator variable for the 1985 episode was used as the exposure variable. In a second approach, continuous concentrations of sulfur dioxide, total suspended particulates, and carbon monoxide were included as exposure variables.

Analyses were conducted separately for men and women to allow for different associations of blood pressure with the covariates.[30] Summary estimates for a joint analysis of men and women were calculated, with adjustment for sex.

Results

Table 1 shows the pollutant concentrations of total suspended particulates, sulfur dioxide, and carbon monoxide during both MONICA surveys (1984–1985 and 1987–1988). Mean concentrations of total suspended particulates and carbon monoxide did not change significantly between the survey periods, but sulfur dioxide concentrations were substantially higher during the first survey in 1984–1985.

As can be seen in Figure 1, the high sulfur dioxide concentrations were caused by a pollution episode between January 7 and January 19, 1985. Sulfur dioxide concentrations rose to a maximum of 238.2 $\mu g/m^3$. Furthermore, the episode was characterized by low temperatures (Figure 1A), stable relative humidity, and easterly winds.[31] Total suspended particulates and sulfur dioxide were moderately correlated ($r = 0.42$) during winter 1984–1985. Carbon monoxide was weakly correlated with sulfur dioxide ($r = 0.28$) but not with total suspended particulates ($r = 0.05$). Winter 1987/1988 was characterized by warmer temperatures compared with winter 1984–1985 (Fig-

TABLE 1—Air Pollution,[a] Temperature,[a] and Systolic Blood Pressure During the Augsburg MONICA Survey (1984–1985) and the Follow-Up (1987–1988)

	N[b]	Mean	SD	Minimum	Maximum
Survey 1984–1985[c]	144	. . .	. . .	. . .	. . .
Total suspended particulates, μg/m^3	119	52.9	32.2	6.8	175.7
Sulfur dioxide, μg/m^3	126	60.2	47.4	13.0	238.2
Carbon monoxide, mg/m^3	126	4.5	1.9	0.9	11.5
Temperature, °C	144	1.9	7.8	–24.8	14.5
Barometric pressure, hPa	144	1015.3	8.3	997.0	1031.0
Follow-up 1987–1988[d]	153				
Total suspended particulates, μg/m^3	131	48.4	22.1	12.0	134.3
Sulfur dioxide, μg/m^3	152	23.8	12.3	5.6	71.1
Carbon monoxide, mg/m^3	153	4.1	1.3	1.7	8.2
Temperature, °C	153	6	6.5	–11.3	18.7
Barometric pressure, hPa	153	1018.5	7.4	998.0	1037.0
Systolic blood pressure, mm Hg					
Men	1339[e]	132	16	89	211
Women	1268[e]	125	18	90	223

Note. HPa = hecto-Pascals; MONICA = World Health Organization project to MONItor trends and determinants in CArdiovascular diseases.
[a]24-hour averages (midnight to midnight).
[b]Number of days out of the days on which subjects were examined.
[c]Examinations on 144 days between October 9, 1984, and May 24, 1985.
[d]Examinations on 153 days between October 16, 1987, and June 24, 1988.
[e]Number of study subjects.

ures 1A and 1B). The correlation between sulfur dioxide and total suspended particulates was similar (r=0.45), and both were correlated with carbon monoxide (r=0.45 and r=0.52, respectively). Barometric pressure remained similar during both surveys.

The mean systolic blood pressure and standard deviation of all study subjects for the first and second survey were 129 (±17) mm Hg and 128 (±17) mm Hg, respectively. Table 1 shows the mean systolic blood pressure stratified by sex. Individuals with an increased heart rate and individuals with an increased plasma viscosity had a higher systolic blood pressure, with a mean and standard deviation of 136 (±18) mm Hg and 137 (±20) mm Hg, respectively. For these analyses, increased heart rate was defined as a heart rate above the 90th percentile, which corresponds to a heart rate greater than 80 beats per minute. Increased plasma viscosity was defined as a plasma viscosity above the 90th percentile in the first survey, which corresponds to plasma viscosity values greater than 1.35 mPa s (milli–Pascal seconds) for men and greater than 1.33 mPa s for women.

In Table 2, the associations between air pollutants, meteorology, and systolic blood pressure in the MONICA surveys are presented. During the air pollution episode, a significant increase in blood pressure was observed in all study subjects after adjustment for cardiovascular risk factors. Further adjustment for temperature, barometric pressure, and relative humidity showed that the change in blood pressure associated with the episode was mainly caused by meteorologic parameters. In men, temperatures below 0°C and barometric pressure had the strongest effect on systolic blood pressure. Women were less affected by barometric pressure than were men. However, relative humidity and temperatures below 0°C and between 0°C and 10°C were associated with a significant change in systolic blood pressure.

Estimates from analyses considering the air pollutant concentrations as continuous variables from both survey periods are also given in Table 2. Regression coefficients are expressed for increases from the 5th to the 95th percentile of each pollutant, and direct comparisons between the estimates are possible. Significant effects for concentrations of sulfur dioxide and total suspended particulates were observed for all study participants. Higher effect estimates for 5-day moving averages compared with effect estimates from the same day for concentrations of total suspended particulates and sulfur dioxide were observed for men and women together. Furthermore, odds ratios (ORs) for an increase in systolic blood pressure above 140 mm Hg, an increase in diastolic blood pressure above 90 mm Hg, or both, were calculated for all study participants (results not shown). The results indicated a significant increase in the risk of attaining a blood pressure reading within the hypertensive range (OR = 1.63; 95% confidence interval [CI] = 1.21, 2.20).

Effect estimates for the association between diastolic blood pressure and air pollution were less in magnitude but also pointed toward an increase in blood pressure in association with total suspended particulates (β=0.81 mm Hg; 95% CI=–0.04, 1.67). No clear association between sulfur dioxide and carbon monoxide and diastolic blood pressure was observed.

When both total suspended particulates and sulfur dioxide were included in the model, the total suspended particulate effect on systolic blood pressure for both men and women remained significant (β=1.75; 95% CI=0.45, 3.05), and the sulfur dioxide effect was substantially reduced (β=0.23; 95% CI=–0.50, 0.96). Adding total suspended particulates and carbon monoxide to the model increased the effect of total suspended particulates on systolic blood pressure from 1.79 mm Hg (95% CI= 0.63, 2.95) to 2.37 mm Hg (95% CI=1.01, 3.72) per increase in total suspended particulates of 90 μg/m^3. No change in effect estimates as compared with the 1-pollutant models occurred when both sulfur dioxide and carbon monoxide were included in the model as exposure variables.

Comparing the effect of total suspended particulates on systolic blood pressure in the city of Augsburg vs the surrounding rural areas showed no difference in the effect estimate for total suspended particulates (β=1.88; 95% CI= 0.15, 3.61 in city of Augsburg vs β=1.73; 95% CI=0.15, 3.31 in the rural areas).

The association between systolic blood pressure and same-day total suspended particulate concentrations in subgroups with high levels of plasma viscosity (>90th percentile) and an increased heart rate (>90th percentile) is presented in Figure 2. The effect estimate shows an increase in systolic blood pressure in all study subjects of 6.93 mm Hg (95% CI=

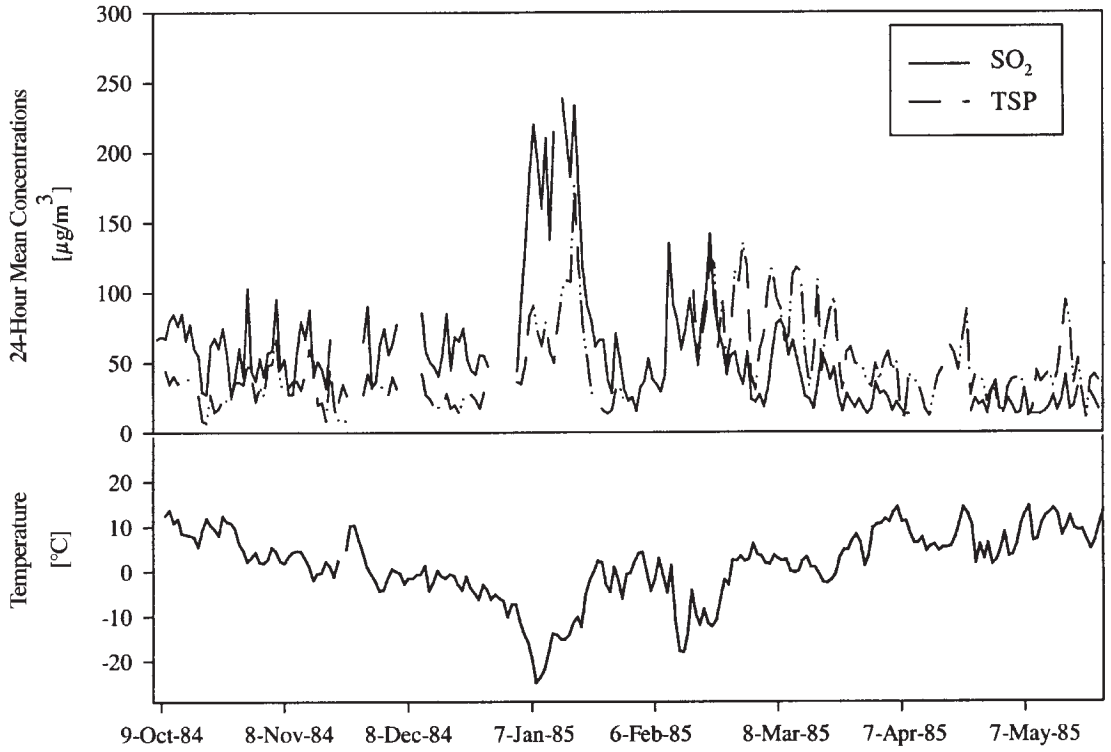

FIGURE 1A—Time series of 24-hour mean total suspended particulates (TSP) and sulfur dioxide (SO_2) concentrations and temperature during the MONICA survey (1984–1985), showing the air pollution episode (January 7 to January 19).

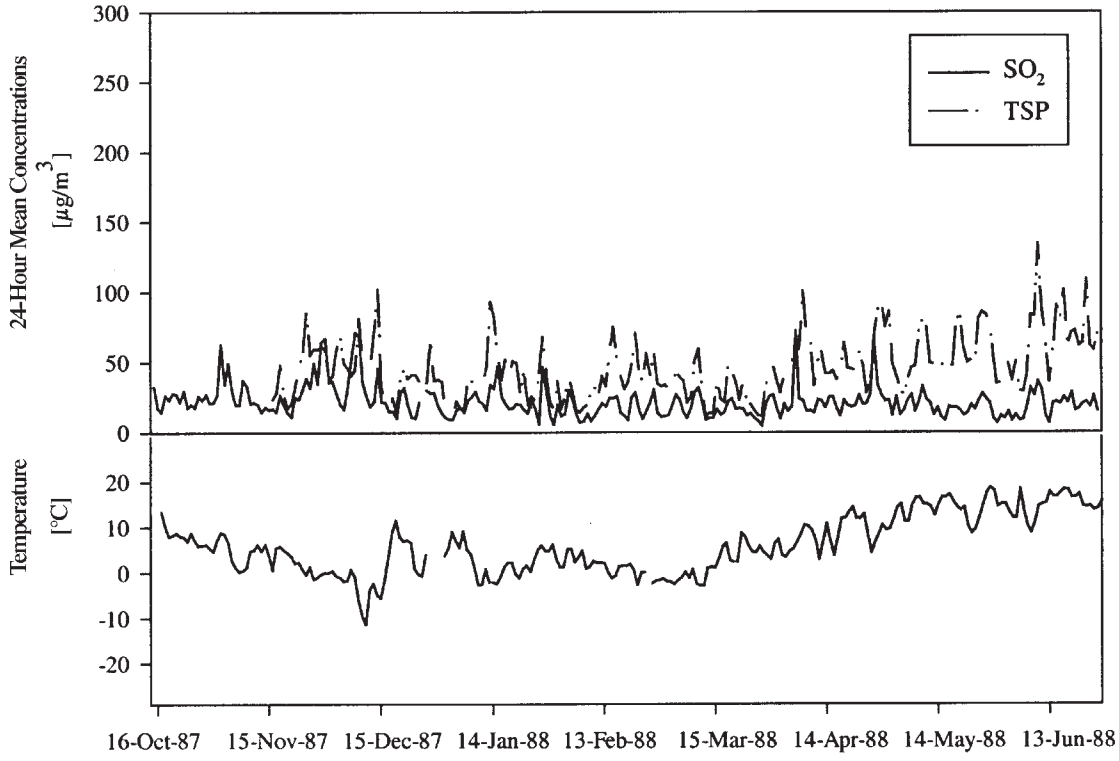

FIGURE 1B—Time series of 24-hour mean total suspended particulates (TSP) and sulfur dioxide (SO_2) concentrations and temperature during the MONICA follow-up (1987–1988).

TABLE 2—Mean Change in Systolic Blood Pressure (SBP) in Association With Air Pollution During the MONICA Cohort Study (N = 2607)

Pollution variable	Men (n = 1339) SBP, mm Hg	95% CI		Women (n = 1268) SBP, mm Hg	95% CI		Men and Women[a] SBP, mm Hg	95% CI	
Crude analysis									
1985 episode[b]	0.88	–1.03	2.79	1.31	–0.86	3.48	1.10	–0.34	2.54
Analysis adjusted for cardiovascular risk factors[c]									
1985 episode[b]	1.58	–0.29	3.47	2.29*	0.11	4.46	1.87*	0.44	3.30
Analyses adjusted for cardiovascular risk factors and meteorologic parameters[d]									
1985 episode[b]	0.20	–1.83	2.24	0.61	–1.73	2.96	0.32	–1.23	1.86
Temperature, <0°C vs ≥0°C	2.81*	1.22	4.40	2.69*	1.02	4.36	2.73*	1.57	3.90
Temperature, 0°C to 10°C vs >10°C	1.27	–0.12	2.66	1.48*	0.03	2.93	1.34*	0.33	2.35
Barometric pressure[e]	–1.38*	–2.62	–0.06	–1.29	–2.71	0.13	–1.30*	–2.34	–0.26
Relative humidity[f]	–0.37	–1.35	0.61	–1.16*	–2.23	–0.09	–0.81*	–1.54	–0.08
Continuous air pollutant concentrations									
Same-day concentrations[d]									
TSP (per 90 μg/m^3)[g]	1.23	–0.31	2.78	2.23*	0.49	3.98	1.79*	0.63	2.95
Sulfur dioxide (per 80 μg/m^3)[g]	0.96*	0.07	1.85	0.96	–0.46	1.49	0.74*	0.08	1.40
Carbon monoxide (per 5.6 mg/m^3)[g]	0.68	–0.94	2.31	0.51	–1.31	2.19	0.53	–0.66	1.72
5-day averages[d]									
TSP (per 70 μg/m^3)[g]	1.05	–0.50	2.61	2.74*	0.89	4.60	1.96*	0.75	3.15
Sulfur dioxide (per 75 μg/m^3)[g]	0.97*	0.09	1.85	1.23*	0.23	2.22	1.07*	0.41	1.73
Carbon monoxide (per 3.6 mg/m^3)[g]	0.92	–0.87	2.70	0.91	–0.87	2.70	1.06	–0.17	2.29

Note. MONICA = World Health Organization project to MONItor trends and determinants in CArdiovascular diseases; CI = confidence interval; TSP = total suspended particulates.
[a]Analyses adjusted for sex.
[b]Compares the SBP during the episode between January 7 and January 19, 1985, with the SBP on all nonepisode days.
[c]Analyses adjusted for age, body mass index, high-density lipoprotein cholesterol, total cholesterol, smoking, leisure-time activity, and medication intake.
[d]Analyses adjusted for temperature, relative humidity, barometric pressure, and cardiovascular risk factors.
[e]Change in barometric pressure from the 5th to the 95th percentile ≅ 26 hPa.
[f]Relative humidity >80% vs relative humidity ≤80%.
[g]Change in pollutant concentration from the 5th to the 95th percentile.
*$P < .05$.

4.31, 9.75) for an increase in total suspended particulates of 90 μg/m^3 in individuals with elevated plasma viscosity levels. An increase in systolic blood pressure of 7.76 mm Hg (95% CI = 5.70, 9.82) was observed for individuals with higher heart rates. Effect estimates of 5-day moving averages of the pollutant concentration were slightly weaker—5.71 mm Hg (95% CI = 3.21, 8.22) for the group with high plasma viscosity and 6.89 mm Hg (95% CI = 5.02, 8.77) for the group with increased heart rates.

Discussion

During the 1985 European air pollution episode, a significant increase in blood pressure was observed in all study subjects after adjustment for cardiovascular risk factors. Further adjustment for low temperature, barometric pressure, and relative humidity indicated that the change in blood pressure associated with the episode was mainly caused by these 3 factors. These results show that not only low temperature and relative humidity but also barometric pressure are important weather variables confounding the association of air pollution and health effects.

Pope et al.[16] found a positive association between barometric pressure and blood oxygen saturation, suggesting that when barometric pressure decreases, oxygen saturation also decreases. This study showed a significant inverse relation between blood pressure and barometric pressure; an increase in blood pressure was associated with a decrease in barometric pressure. Thus, a decrease in barometric pressure might decrease blood oxygen saturation and increase blood pressure. A decrease in blood oxygen saturation could be an indicator for hypoxia, which could alter autonomic regulation.

Another analysis by Pope et al.[32] on mortality data and air pollution found that barometric pressure was negatively associated with total and cardiovascular mortality. These findings indicate that barometric pressure might have a considerable effect on the cardiovascular system. Therefore, barometric pressure might be a potential confounder in the association between cardiovascular morbidity and mortality and air pollution.

The results of the analysis that used continuous air pollution variables over both survey periods suggested that elevated 24-hour concentrations of ambient total suspended particulates and sulfur dioxide were associated with an increase in systolic blood pressure in a random sample of men and women. Even after adjustment for other cardiovascular risk factors and meteorologic parameters, the increase in systolic blood pressure remained significant. Unfortunately, no data on the concentrations of fine and ultrafine particles were available, and sulfur dioxide and total suspended particulates served as surrogates for the levels of inhalable particles. The results of the 2-pollutant models indicated that the total suspended particulate effect clearly dominates the sulfur dioxide effect. This suggests that the association between systolic blood pressure and air pollution is attributable more to the effect of the particulate matter than to the effect of sulfur dioxide.

Little information is available on underlying biological mechanisms to explain an increase in systolic blood pressure in association with particulate air pollution. A study on acute effects of inhaled urban air pollution particles in rats[33]

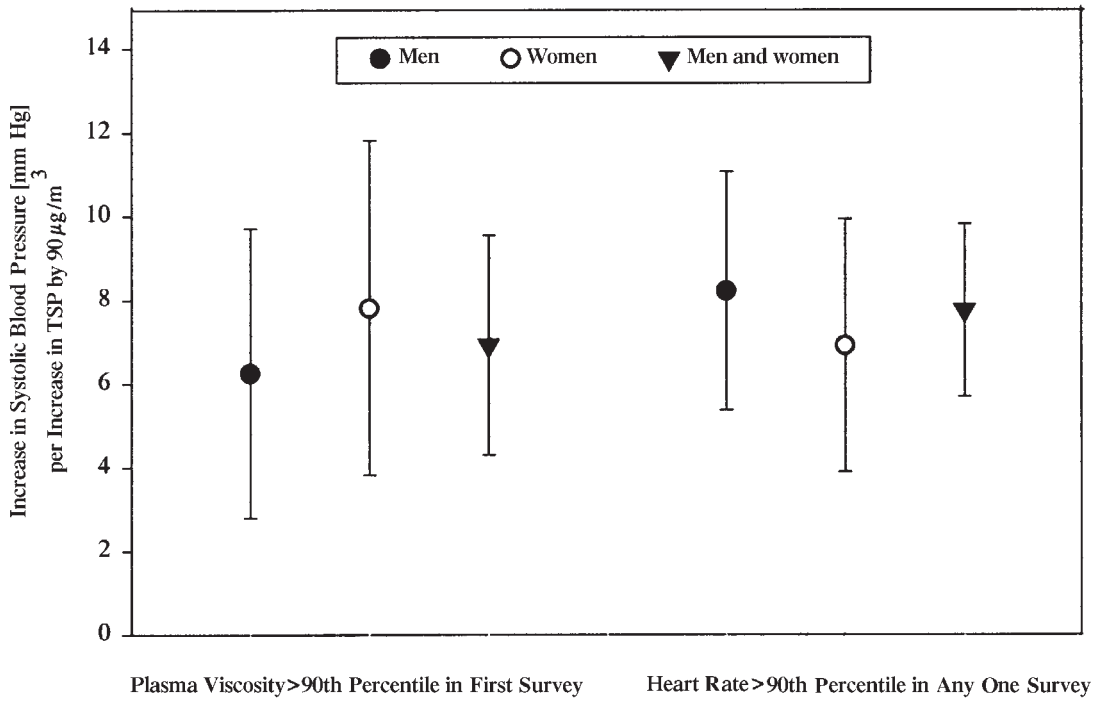

FIGURE 2—Mean change in systolic blood pressure in association with same-day total suspended particulates (TSP) in subjects with high levels of plasma viscosity and increased heart rate.

showed increased plasma levels of endothelin-1, which is thought to play an active role in the maintenance of basal systemic vascular tone. These findings were based on the hypothesis that respirable particles are able to access the distal alveolar surface area and affect the lung capillaries through bioavailable components leaching from the particles. The generation of endothelin-1 is markedly increased by hypoxia and free radicals[34] and could therefore be increased in lung capillaries through oxidative damage caused by respirable particles.

In animal models, injection of endothelin-1 caused dose-related increases in sympathetic nerve activity and blood pressure. It also has been reported that endothelin-1 may act on the central nervous system as a neurotransmitter or neuromodulator. As a consequence, it might participate in cardiovascular regulation through the central nervous system, and an alteration in the central endothelin-1 system could result in blood pressure elevation.[35] Evidence indicates that activation of the sympathetic nervous system plays an important role in hypertension and parallels the degree of blood pressure elevation.[36] However, most of these studies have been conducted with animal models, and these potential mechanisms still must be confirmed in the human organism.

Recent epidemiologic studies[17–19] assessing the association between autonomic cardiac function and particulate air pollution found an alteration in heart rate variability in association with an increase in particulate matter. Even though findings from Gold et al.[19] and Pope et al.[18] differ with respect to the particle effects on parasympathetic function, these findings support the hypothesis of the alteration of the autonomic nervous system in association with particulate matter.

In a retrospective analysis of the Augsburg data, Peters et al.[23] found an association between elevated levels of plasma viscosity and total suspended particulates. Plasma viscosity was positively associated with blood pressure in the MONICA population.[37] Furthermore, heart rate increased in association with total suspended particulates, sulfur dioxide, and carbon monoxide.[24] In our analysis, increases in blood pressure in association with total suspended particulates were 4 times higher for men and women with an increased heart rate. Similar increases in the magnitude of the effects were observed in a subgroup of individuals with increased plasma viscosity. These results show that individuals with other cardiovascular risk factors might be more susceptible to systemic changes than are individuals without these risk factors.

Analyses of emergency hospital admissions and mortality in association with ambient air pollution showed increased hospital admissions, particularly for acute coronary syndromes and arrhythmia.[3,21] A clear increase in cardiovascular death occurred in association with ambient air pollution.[38] Given these results, one would expect to see systemic changes in the cardiovascular system resulting in adverse cardiac events. Blood pressure, plasma viscosity, heart rate, and heart rate variability are significant predictors of cardiovascular mortality and morbidity and adverse cardiac outcomes. Overall, current findings support the hypothesis of the alteration of the autonomic nervous system and humoral response in association with particulate air pollution.

Blood pressure is an extremely variable parameter and depends on factors such as medication, exercise, age, sex, and meteorology, for which we tried to adequately control in this analysis, but we still must be careful in interpreting these results. A further limitation of the study is the use of air quality data from a single central measuring site to estimate exposure to air pollutants. However, the effect of this limitation would be random misclassification of exposure, which would not be expected to produce a false-positive association.

Our results showed a consistent significant increase in blood pressure in a random sample of men and women in association with increased concentrations of total suspended particulates. Furthermore, a significant increase

in the risk of attaining a blood pressure within the hypertensive range was observed. Since an increase in blood pressure could be caused by a change in cardiovascular autonomic control, which could indeed influence adverse cardiac events, it is important to understand the effects of particulate air pollution on the autonomic nervous system. All potential risk factors for cardiovascular mortality and morbidity need to be identified. Further research applying other methods, such as time-series studies, is needed to investigate the effects of ambient particulate matter on cardiovascular health. □

Contributors

A. Ibald-Mulli reanalyzed the data and wrote the paper. J. Stieber was involved in the design, fieldwork, and analysis of the initial MONICA Augsburg survey. She assisted with the interpretation of the current results. H.-E. Wichmann contributed to the writing of the paper. W. Koenig was involved in the analysis of the MONICA survey and contributed to the writing of the paper. A. Peters proposed the topic, supervised data analysis and interpretation, and contributed to the writing of the paper.

References

1. Schwartz J. Air pollution and daily mortality: a review and meta analysis. *Environ Res*. 1994; 64:36–52.
2. Thurston GD. A critical review of PM10-mortality time-series studies. *J Expo Anal Environ Epidemiol.* 1996;6:3–21.
3. Burnett RT, Smith-Doiron M, Stieb D, Cakmak S, Brook JR. Effects of particulate and gaseous air pollution on cardiorespiratory hospitalizations. *Arch Environ Health.* 1999;54:130–139.
4. Borja-Aburto VH, Castillejos M, Gold DR, Bierzwinski S, Loomis D. Mortality and ambient fine particles in southwest Mexico City, 1993–1995. *Environ Health Perspect.* 1998;106: 849–855.
5. Dab W, Medina S, Quenel P, et al. Short term respiratory health effects of ambient air pollution: results of the APHEA project in Paris. *J Epidemiol Community Health.* 1996;50(suppl 1): S42–S46.
6. Delfino RJ, Becklake MR, Hanley JA. The relationship of urgent hospital admissions for respiratory illnesses to photochemical air pollution levels in Montreal. *Environ Res.* 1994;67:1–19.
7. Pope CA III, Bates DV, Raizenne ME. Health effects of particulate air pollution: time for reassessment? *Environ Health Perspect.* 1995;103: 472–480.
8. Prescott GJ, Cohen GR, Elton RA, Fowkes FG, Agius RM. Urban air pollution and cardiopulmonary ill health: a 14.5 year time series study. *Occup Environ Med.* 1998;55:697–704.
9. Schwartz J. Air pollution and hospital admissions for heart disease in eight US counties. *Epidemiology.* 1999;10:17–22.
10. Sheppard L, Levy D, Norris G, Larson TV, Koenig JQ. Effects of ambient air pollution on nonelderly asthma hospital admissions in Seattle, Washington, 1987–1994. *Epidemiology.* 1999;10:23–30.
11. Spix C, Wichmann HE. Daily mortality and air pollutants: findings from Köln, Germany. *J Epidemiol Community Health.* 1996;50(suppl): S52–S58.
12. Zmirou D, Schwartz J, Saez M, et al. Time-series analysis of air pollution and cause-specific mortality. *Epidemiology.* 1998;9:495–503.
13. Seaton A, MacNee W, Donaldson K, Godden D. Particulate air pollution and acute health effects. *Lancet.* 1995;345:176–178.
14. Godleski JJ, Sioutas C, Kalter M, Koutrakis P. Death from inhalation of concentrated ambient particles in animal models of pulmonary disease [abstract]. *Am J Respir Crit Care Med.* 1996; 153:A15.
15. Godleski JJ, Sioutas C, Verrier RL, et al. Inhalation exposure of canines to concentrated ambient air particles [abstract]. *Am J Respir Crit Care Med.* 1997;155:A246.
16. Pope CA, Dockery DW, Kanner RE, Villegas GM, Schwartz J. Oxygen saturation, pulse rate, and particulate air pollution: a daily time-series panel study. *Am J Respir Crit Care Med.* 1999; 159:365–372.
17. Liao D, Creason J, Shy C, Williams R, Watts R, Zweidinger R. Daily variation of particulate air pollution and poor cardiac autonomic control in the elderly. *Environ Health Perspect.* 1999;107: 521–525.
18. Pope CA III, Verrier AL, Lovett EG, et al. Heart rate variability associated with particulate air pollution. *Am Heart J.* 1999;138:890–899.
19. Gold DR, Litonjua A, Schwartz J, et al. Ambient pollution and heart rate variability. *Circulation.* 2000;101:1267–1273.
20. de Leeuw FA, Leyssius HJ. Long-range transport modeling of air pollution episodes. *Environ Health Perspect.* 1989;79:53–59.
21. Wichmann HE, Mueller W, Allhoff P, et al. Health effects during a smog episode in West Germany in 1985. *Environ Health Perspect.* 1989;79:89–99.
22. Keil U, Stieber J, Döring A, et al. The cardiovascular risk factor profile in the study area Augsburg: results from the first MONICA survey 1984/ 85. *Acta Med Scand Suppl.* 1988;728:119–128.
23. Peters A, Döring A, Wichmann HE, Koenig W. Increased plasma viscosity during an air pollution episode: a link to mortality? *Lancet.* 1997; 349:1582–1587.
24. Peters A, Perz S, Döring A, Stieber J, Koenig W, Wichmann HE. Increases in heart rate during an air pollution episode. *Am J Epidemiol.* 1999; 150:1094–1098.
25. Welin L, Eriksson H, Larsson B, Svardsudd K, Wilhelmsen L, Tibblin G. Risk factors for coronary heart disease during 25 years of follow-up: the study of men born in 1913. *Cardiology.* 1993;82:223–228.
26. World Health Organization. *MONICA Manual*. Geneva, Switzerland: World Health Organization; 1990.
27. Kirkendall WM, Feinleib M, Freis ED, Mark AL. Recommendations for human blood pressure determination by sphygmomanometers. *Hypertension.* 1981;3:510A–519A.
28. Hense HW, Koivisto AM, Kuulasmaa K, Zaborskis A, Kupsc W, Tuomilehto J. Assessment of blood pressure measurement quality in the baseline surveys of the WHO MONICA project. *J Hum Hypertens.* 1995;9:935–946.
29. Chalmers J, MacMahon S, Mancia G, et al. 1999 World Health Organization–International Society of Hypertension Guidelines for the management of hypertension: guidelines subcommittee. *Clin Exp Hypertens.* 1999;21: 1009–1060.
30. Koenig W, Sund M, Lowe GDO, et al. Geographical variations in plasma viscosity and relation to coronary event rates. *Lancet.* 1994;344: 711–714.
31. Burnett RT, Cakmak S, Brook JR, Krewski D. The role of particulate size and chemistry in the association between summertime ambient air pollution and hospitalization for cardiorespiratory diseases. *Environ Health Perspect.* 1997; 105:614–620.
32. Pope CA III, Hill RW, Villegas GM. Particulate air pollution and daily mortality on Utah's Wasatch Front. *Environ Health Perspect.* 1999; 107:567–573.
33. Bouthillier L, Vincent R, Goegan P, et al. Acute effects of inhaled urban particles and ozone: lung morphology, macrophage activity, and plasma endothelin-1. *Am J Pathol.* 1998;153: 1873–1884.
34. Haynes WG, Webb DJ. Endothelin as a regulator of cardiovascular function in health and disease. *J Hypertens.* 1998;16:1081–1098.
35. Nakamura K, Sasaki S, Moriguchi J, et al. Central effects of endothelin and its antagonists on sympathetic and cardiovascular regulation in SHR-SP. *J Cardiovasc Pharmacol.* 1999;33: 876–882.
36. Grassi G. Role of the sympathetic nervous system in human hypertension. *J Hypertens.* 1998; 16(12 pt 2):1979–1987.
37. Koenig W, Sund M, Ernst E, Keil U, Rosenthal J, Hombach V. Association between plasma viscosity and blood pressure: results from the MONICA-project Augsburg. *Am J Hypertens.* 1991;4: 529–536.
38. Wichmann H-E, Spix C, Tuch T, et al. Daily mortality and fine and ultrafine particles in Erfurt, Germany, I: role of particle number and particle mass. Cambridge, Mass: Health Effects Institute; November 2000. Report 98.