A Study of Twelve Southern California Communities with Differing Levels and Types of Air Pollution

II. Effects on Pulmonary Function

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To study the possible chronic respiratory effects of air pollutants, we designed and initiated a 10-yr prospective study of Southern California public schoolchildren living in 12 communities with different levels and profiles of air pollution. The design of the study, exposure assessment methods, and survey methods and results related to respiratory symptoms and conditions are described in the accompanying paper. Pulmonary function tests were completed on 3,293 subjects. We evaluated cross-sectionally the effects of air pollution exposures based on data collected in 1986–1990 by existing monitoring stations and data collected by our study team in 1994. Expected relationships were seen between demographic, physical, and other environmental factors and pulmonary function values. When the data were stratified by sex, an association was seen between pollution levels and lower pulmonary function in female subjects, with the associations being stronger for the 1994 exposure data than the 1986–1990 data. After adjustment, PM_{10}, $PM_{2.5}$, and NO_2 were each significantly associated with lower FVC, FEV_1, and maximal midexpiratory flow (MMEF); acid vapor with lower FVC, FEV_1, peak expiratory flow rate (PEFR), and MMEF; and O_3 with lower PEFR and MMEF. Effects were generally larger in those girls spending more time outdoors. Stepwise regression of adjusted pulmonary function values for girls in the 12 communities showed that NO_2 was most strongly associated with lower FVC ($r = -0.74$, $p < 0.01$), $PM_{2.5}$ with FEV_1 ($r = -0.72$, $p < 0.01$), O_3 with PEFR ($r = -0.75$, $p < 0.005$), and $PM_{2.5}$ with MMEF ($r = -0.80$, $p < 0.005$). There was a statistically significant association between ozone exposure and decreased FVC and FEV_1 in girls with asthma. For boys, significant associations were seen between peak O_3 exposures and lower FVC and FEV_1, but only in those spending more time outdoors. These findings underline the importance of follow-up of this cohort. **Peters JM, Avol E, Gauderman WJ, Linn WS, Navidi W, London SJ, Margolis H, Rappaport E, Vora H, Gong H, Jr, Thomas DC. A study of twelve Southern California communities with differing levels and types of air pollution: II. Effects on pulmonary function.**

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Portions of Southern California experience severe air pollution, with high levels of ozone (O_3), particulate matter (measured as PM_{10}), nitrogen dioxide (NO_2), and strong acid vapor, separately or in combination. Some evidence suggests increased risk of chronic respiratory disease in this environment

(1, 2), but long-term health consequences for local residents remain uncertain, particularly for children. To help understand long-term effects in children, we designed and instituted a 10-yr study of respiratory health and air pollution exposure in public school students from 12 middle-income Southern California communities with a broad range of air quality. The study's rationale and objectives are described more fully in the previous paper (3), which also includes results of air monitoring and subjective assessments of respiratory symptoms from questionnaires. To examine the possible chronic deleterious effects of air pollution in Southern California, we analyzed the relationship between air pollution levels and cross-sectional pulmonary function test results in 3,293 subjects.

METHODS

Experimental Design

As described previously (3), the study was based on a quasi-factorial design that focused on O_3, PM_{10}, NO_2, and acid vapor as the pollutants

of primary interest. Selection of communities with high and low levels of each pollutant, subject recruitment, exposure estimation, and survey methods to assess demographic, household, activity, and baseline medical characteristics are also described in the previous paper. We sought to recruit approximately 150 children in grade 4, 75 in grade 7, and 75 in grade 10 from each community, for a total study population of 3,600.

Health Effects Assessment

A questionnaire concerning medical history, residential history, and housing characteristics was filled out by subjects' parents during the winter of 1993. A second questionnaire concerning typical physical activity and time spent outdoors was administered in the spring of 1993 during lung function testing. It was answered by subjects themselves, with assistance from parents if needed.

Lung function testing was scheduled during the morning hours of spring in order to avoid daily and annual peak pollution levels, which occur most often during summer or autumn afternoons. Maximum forced expiratory flow–volume maneuvers were recorded using rolling-seal spirometers (Spiroflow; P.K. Morgan Ltd., Gillingham, UK) interfaced to personal computers. Testing and data management procedures were similar to those in the Six Cities Study (4). Each subject was asked to perform three satisfactory blows, defined as FVC and FEV_1 agreeing within 5%, FEV_1 extrapolation volume less than 100 ml or 5% of FVC, less than 50 ml expired in the final 2 s, and forced expiratory time exceeding 3 s. These criteria are based on American Thoracic Society recommendations (5), modified for children. No more than seven blows were attempted. The subject was questioned privately regarding smoking habits, recent illness, or recent exercise, which might affect test results. To predict subjects' lung function, height and weight were measured at the time of testing, with shoes and coats removed, while age, gender, and ethnicity were determined from parents' questionnaire responses.

Six trained lung function technicians performed the testing, using six different spirometers. To promote uniformly high quality of technician performance, unannounced quality assurance inspections were conducted in the field about three times per month; data were reviewed and feedback was provided to individual technicians concerning the overall quality of their subjects' performance, as judged by the aforementioned criteria for satisfactory blows. Each community was visited two or three times, at intervals of 1 mo or longer, with no more than half its subjects being tested at one visit. This minimized the potential influence of intercurrent pollution episodes, respiratory infection outbreaks, or other short-term confounders. In all, lung function data were obtained from 3,293 (90%) subjects.

Spirometers' calibrations were checked just before, during, and just after each morning's testing session using flow–volume syringes (Jones Medical Instrument Co., Oak Brook, IL). Although all spirometers performed consistently within American Thoracic Society specifications (5), their volume readings occasionally shifted by 1–2%. Volume variability was significantly less between syringes than between spirometers (6). Accordingly, we adjusted each subject's spirometric data, multiplying each raw measurement by the median of syringe FVC/spirometer FVC ratios recorded at the calibration checks most closely preceding and following the subject's test session. Nevertheless, subsequent multiple regression analyses showed that spirometer and technician differences contributed significantly to the variance of lung function data. Therefore, dummy variables representing individual spirometers and technicians were included in the statistical models.

Statistical Methods

Let Y_{ij} be a pulmonary function test (PFT) measure (FVC, FEV_1, maximal midexpiratory flow [MMEF], or peak expiratory flow rate [PEFR]) on the ith child in the jth community, and let X_{ij} denote a set of personal variables such as sex, race, height, and age as well as those described in Table 5 in the comparison paper (3). Stepwise multiple regression was utilized to determine which personal variables were significantly correlated with each PFT, after adjustment for community, grade in school, technician, and spirometer. The personal covariates that were significant at the $p < 0.15$ level for a given PFT measure were included in all subsequent models of pollutant effects. To account for differential patterns of lung growth with respect to sex and age, we included interaction terms of sex with grade, and sex and grade with age, race, height, and weight in all models of pollutant effects.

To investigate the relationship between PFT and air pollutants, we used a two-stage regression approach. In the first stage, we fit the following multiple regression model:

$$Y_{ij} = \mu_j + \gamma X_{ij} + e_{ij} \qquad (1)$$

in which μ_j represents the mean PFT for community j, adjusted for the personal variables, and e_{ij} is an error term assumed to be normally distributed. The adjusted community means were then utilized in a second ("ecologic") model of the form

$$\mu_j = \alpha + \beta Z_j + e_j \qquad (2)$$

where Z_j is the level of some pollutant for community j, and e_j is an error term assumed to be normally distributed. The parameter of interest is β, the slope coefficient for the relationship between community mean PFT and pollutant level. Since the numerical scale of measure is different among the various pollutants, we standardize each to its interquartile range across communities, so that it reflects the expected difference in lung function between the 25th and 75th percentiles of exposure to the corresponding pollutant.

For each PFT, we checked the distribution of residuals from the first stage model for normality, both visually using histograms and statistically using the Kolmogorov D-statistic. Within males and females, the distribution of residuals was bell-shaped and passed the Kolmogorov test of normality. For all subjects combined, the residuals also followed a bell shape, but the null hypothesis of normality was rejected at $p < 0.01$. For comparison, we tried a log-transform of each outcome and found that within males and females, the residuals were slightly less normally distributed, although they still passed the Kolmogorov test. In all subjects combined, the null hypothesis of normality of the residuals for the log-transformed data was also rejected at $p < 0.01$. It is common when samples sizes are large (such as in all subjects combined) to reject the hypothesis of normality, since the corresponding power to detect very slight deviations from normality is high. Thus, we did not find compelling evidence that a transformation should be made, and all analyses were conducted on raw (untransformed) PFT values.

For the model in Equation 2, we considered pollutant levels from two different calendar periods. The first measures cover the period 1986–1990 and were computed as the 5-yr average of the year-specific annual averages. The four pollutants considered were peak (1-h maximum) ozone, and 24-h averages of PM_{10}, NO_2, and acid (HCl + HNO_3). These metrics were the ones utilized in the original selection process for the study. The second set of pollutant measures are derived for calendar year 1994, the first year for which we have complete on-study air monitoring data. In addition to the four pollutants described above, we computed annual averages of 24-h average $PM_{2.5}$ (mass) and 24-h ozone.

The above models were applied to all subjects in the data set and to subsets defined by sex. Since the pollutant measures represent outdoor ambient levels, we also wanted to determine whether the amount of time spent outdoors modified the PFT–pollutant relationship. At entry to the study, subjects were asked how many hours they spent outdoors over the previous 2-wk period. Responses to this question were utilized to stratify subjects into either the "more outdoors" group or "less outdoors" group, based on whether they were above or below the median for their respective community, sex, and grade cohort. Regression analyses of pollutant effects were then performed separately for each of the two groups. In analyses of PFT–pollutant relationships, two-sided p values greater than 0.05 are reported as nonsignificant. Using similar methodology, we also stratified the sample based on asthma status (doctor diagnosed) and by migrant status. For the latter, migrants were defined as children who lived at least 7% of their lives outside of their current community.

RESULTS

Community Comparisons

We achieved a 90% participation rate (range, 82–96%) in the lung function testing and an 83% (range, 72–90%) response rate from the activity questionnaire.

The correlations between potential confounders and pul-

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TABLE 1

PARTIAL CORRELATIONS OF LUNG FUNCTION MEASUREMENTS WITH POTENTIAL CONFOUNDERS

Variable	FVC	FEV_1	PEFR	MMEF
Age	0.04*	0.04†	0.08†	0.04*
Male vs. Female	0.30†	0.20*	0.11*	−0.04*
Black vs. White	−0.17†	−0.20†	−0.01‡	−0.08†
Asian vs. White	−0.08†	−0.05†	0.05*	0.02‡
Other vs. White	0.01‡	0.02‡	0.02‡	0.04†
Hispanic	0.04*	0.04*	0.03	0.02
Height	0.19†	0.22†	0.13†	0.10†
Weight	0.19†	0.14†	0.08†	0.05*
Body mass	−0.13†	−0.10†	−0.07†	−0.04†
Ever asthma	0.00	−0.09†	−0.03†	−0.06†
Recent asthma	0.00	−0.02	−0.02	−0.05†
Hay fever	0.00	−0.02	−0.02	−0.03†
Passive smoke	0.00	−0.02	−0.08†	−0.03*
Active smoking	0.08†	0.05†	0.04†	0.00
Recent exercise	0.01	−0.01	−0.03*	−0.01
Cats	0.04†	0.03†	0.01	−0.01
Pets	0.01	0.03	0.05†	0.01
Gas stove	−0.07†	−0.06†	−0.04†	−0.03
Total R^2	0.87	0.86	0.73	0.59

Definition of abbreviations: PEFR = peak expiratory flow rate; MMEF = maximal mid-expiratory flow.

* $p < 0.15$.
† $p < 0.05$.
‡ This category of race was not significantly different than white at the 0.15 level. However, it was included in all subsequent models as a component of race adjustment.

Items with asterisks and daggers are included in the final adjustment model for this measurement. These items are adjusted for each other; remaining variables are adjusted only for the variables with asterisks and daggers. All models are adjusted for community, grade in school, spirometer, and technician. The total R^2 for each outcome is computed for the model with these latter adjustment variables and the variables with asterisks and daggers.

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TABLE 2

REGRESSION OF PULMONARY FUNCTION TESTS (PFT) ON 1986–1990 AMBIENT AIR POLLUTANTS*

PFT Pollutant†	All Subjects ($n = 2,781$)		Males Only ($n = 1,424$)		Females Only ($n = 1,357$)	
	B	SE	B	SE	B	SE
FVC						
Peak O_3	−2.7	(18.0)	26.9	(24.3)	−21.9	(21.6)
PM_{10}	−24.9	(11.4)‡	−9.9	(19.6)	−39.3	(12.3)§
NO_2	−42.6	(13.5)‡	−27.6	(25.9)	−58.5	(15.4)‖
Acid	−24.9	(20.5)	4.5	(31.4)	−45.6	(23.6)
FEV_1						
Peak O_3	−3.8	(13.6)	24.4	(19.4)	−29.7	(15.0)
PM_{10}	−15.7	(9.3)	3.6	(16.1)	−34.2	(8.3)‖
NO_2	−23.2	(12.5)	−7.6	(22.1)	−39.9	(13.9)*
Acid	−7.0	(16.5)	21.7	(24.6)	−34.2	(18.7)
PEFR						
Peak O_3	−94.2	(28.3)§	31.1	(48.8)	−187.2	(50.1)‖
PM_{10}	−43.8	(28.4)	23.3	(37.7)	−110.9	(48.4)*
NO_2	−19.0	(43.2)	48.0	(50.6)	−109.2	(74.8)
Acid	−22.5	(49.6)	93.0	(53.1)	−119.1	(86.8)
MMEF						
Peak O_3	−51.9	(14.7)§	11.7	(26.7)	−102.2	(28.8)§
PM_{10}	−32.0	(13.7)‡	19.9	(19.8)	−85.0	(19.8)‖
NO_2	−27.5	(21.7)	23.0	(27.6)	−90.1	(36.1)*
Acid	−7.9	(26.8)	6.3	(32.8)	−32.3	(51.2)

For definition of abbreviations, *see* Table 1.

* Single pollutant models adjusted for personal and environmental factors. Models for all subjects are adjusted for the variables footnoted by ‡, §, and ‖ in Table 2, the variables listed in the footnote of this table, $height^2$, $weight^2$, the two-way interaction of sex and grade with age, race, height, $height^2$, weight, and $weight^2$. Models for females and males are adjusted for the same variables except those involving sex.

† Regression coefficients are scaled to the interquartile range for each pollutant as follows: 40 ppb of O_3, 25 μg/m^3 of PM_{10}, 25 ppb of NO_2, and 1.7 ppb of acid (HCl + HNO_3, measured on a mole basis). Four models are fit for each pulmonary function test, one for each pollutant.

‡ $p < 0.05$.
§ $p < 0.01$.
‖ $p < 0.005$.

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monary function results are presented in Table 1. Previously observed relationships are present in this data set. Age, height, weight, gender, race, and asthmatic status are important. Passive smoking was associated with decreased expiratory flow rates and active smoking with increased FVC, FEV_1 and PEFR. Presence of a gas stove was associated with uniformly lower lung function. In the analysis of pollutant effects, items with asterisks and daggers are included in the first stage model (Equation 1). A considerable amount of variation is accounted for by these factors with an R^2 of 0.86 for FEV_1 and 0.87 for FVC.

The percent predicted pulmonary function tests for the 12 communities were computed for each pulmonary function test value based on the regression models shown in Table 1. For all subjects, there was a statistically significant difference of FVC as a percent predicted across the communities. When all subjects were divided by sex, the girls showed greater community variation than boys, with significant differences for both FVC and FEV_1.

The results of adjusted pulmonary function tests regressed on 1986–1990 ambient air pollution data are presented in Table 2 for all subjects, males and females. We found statistically significant relationships between air pollution level and pulmonary function tests in females only. Peak O_3 was associated with negative effects on MMEF and PEFR. PM_{10} had strong associations with decreased FVC, FEV_1, and MMEF. NO_2 was associated with decreases in FVC, FEV_1, and MMEF. Although regression coefficients for acid were also negative for females, none achieved statistical significance.

A similar presentation is made for the 1994 air pollution data in Table 3. Again, significant effects were seen only in females. In general, the coefficients were larger, and now the

associations with acid exposure were statistically significant for all measures of pulmonary function. $PM_{2.5}$ exposure was associated with statistically significant decreases in all four measures of pulmonary function, and the associations were stronger than for PM_{10}. However, 24-h average O_3 was not significantly correlated with any of the pulmonary function test values (data not shown).

We performed additional multivariate modeling of the female data to determine which of the 1994 pollutants was most correlated with each PFT. The strongest univariate correlations for each PFT were NO_2 for FVC, acid vapor for FEV_1, peak O_3 for PEFR, and $PM_{2.5}$ for MMEF. For each of the outcomes, the pollutant explains at least 55% of the variability in community-specific adjusted PFTs. The relationships between pollution levels and pulmonary function outcome were quite similar for some of the pollutants, raising the question of whether the effects can be separated. To examine this question, we regressed the adjusted pulmonary function measurements on 1994 ambient pollutants, two pollutants at a time. For FVC, FEV_1, and PEFR, no two-pollutant models fit significantly better than the best single pollutant model. For MMEF, however, O_3 in combination with either PM_{10} or NO_2 fit better than the best single pollutant ($PM_{2.5}$). Of these two 2-pollutant models, the best-fitting one included peak O_3 and PM_{10}, with regression coefficients (B) of −89.2 ($p < 0.05$) and −86.8 ($p < 0.01$), respectively.

In Table 4, we stratified the data at the median for each sex by time spent outdoors to determine whether the effects are

TABLE 3

REGRESSION OF PULMONARY FUNCTION TESTS (PFT) ON 1994 AMBIENT AIR POLLUTANTS*

PFT Pollutant[†]	All Subjects		Males Only		Females Only	
	B	SE	B	SE	B	SE
FVC						
Peak O_3	7.9	(24.4)	50.8	(31.2)	−19.1	(30.3)
PM_{10}	−26.8	(17.3)	−7.4	(27.5)	−45.8	(19.5)[‡]
$PM_{2.5}$	−31.8	(18.7)	−7.5	(30.2)	−56.7	(19.8)[‡]
NO_2	−46.2	(16.0)[‡]	−29.9	(29.5)	−63.8	(18.3)[§]
Acid	−23.0	(13.9)	3.4	(22.4)	−44.0	(14.0)[‡]
FEV1						
Peak O_3	−1.6	(18.6)	36.7	(26.1)	−36.6	(21.2)
PM_{10}	−16.5	(13.7)	8.1	(22.3)	−40.6	(14.0)[‡]
$PM_{2.5}$	−19.6	(14.8)	8.3	(24.5)	−47.6	(14.4)[§]
NO_2	−22.3	(14.8)	−2.1	(25.1)	−44.1	(16.1)[‡]
Acid	−13.9	(11.0)	8.2	(18.0)	−36.2	(10.3)[§]
PEFR						
Peak O_3	−128.3	(38.5)[§]	52.0	(65.8)	−250.9	(69.9)[‖]
PM_{10}	−56.9	(40.2)	37.1	(52.0)	−157.0	(66.8)[‡]
$PM_{2.5}$	−59.7	(44.6)	46.0	(56.8)	−170.9	(73.7)[‡]
NO_2	−29.5	(48.5)	54.2	(57.3)	−133.4	(83.1)
Acid	−49.5	(32.2)	47.5	(40.6)	−139.7	(51.1)[‡]
MMEF						
Peak O_3	−69.5	(20.5)[§]	−25.1	(35.8)	−124.7	(44.0)[‡]
PM_{10}	−38.7	(20.2)	26.6	(27.6)	−109.4	(31.0)[§]
$PM_{2.5}$	−46.3	(21.5)	32.0	(30.1)	−130.0	(30.3)[‖]
NO_2	−32.9	(24.4)	30.0	(30.9)	−109.5	(38.9)[‡]
Acid	32.0	(16.3)	0.3	(23.4)	−75.5	(29.2)[‡]

For definition of abbreviations, *see* Table 1.

* Adjusted for personal and environmental factors. Models for all subjects are adjusted for the variables footnoted by [†], [§], and [‖] in Table 3, the variables listed in the footnote of this table, height[²], weight[²], the two-way interaction of sex and grade with age, race, height, height[²], weight, and weight[²]. Models for females and males are adjusted for the same variables except those involving sex.

[†] Regression coefficients are scaled to the interquartile range for each pollutant as follows: 40 ppb of O_3, 25 $\mu g/m^3$ of PM_{10}, 15 $\mu g/m^3$ of $PM_{2.5}$, 25 ppb of NO_2, and 1.7 ppb of acid (HCl + HNO_3, measured on a mole basis). Four models are fit for each pulmonary function test, one for each pollutant.

[‡] $p < 0.05$.
[§] $p < 0.01$.
[‖] $p < 0.005$.

greater in those subjects who spend more time outdoors. For both boys and girls, coefficients were generally more negative for those subjects spending more time outdoors. For boys, those spending more time outdoors had statistically significant negative association between peak O_3 and both FVC and FEV_1.

We included three grade levels in this cross-sectional study to determine whether older children, because of their longer exposure, have greater effects. To address this question, we tested for trends in coefficients across the three age groups in each gender separately, but found no significant or consistent patterns, although for FEV_1 the coefficients were largest for the older female subjects.

We stratified the data by asthmatic status for male and female subjects (Table 5). For girls with asthma, O_3 exposure was significantly associated with decreases in FVC and FEV_1, and PM_{10} and $PM_{2.5}$ were significantly associated with decreases in PEFR. All pollutant measures were associated with larger negative coefficients for PEFR in girls with asthma. For boys, there was no statistically significant negative association. A statistically significant increase in PEFR was associated with peak O_3 exposure.

Not all subjects spent their entire lives in the community in which they were residing at the time of this study. We therefore analyzed the data on life-long residents versus others. The negative associations between air pollution measurements and

pulmonary function outcomes did not differ significantly between life-long residents and others (data not shown).

DISCUSSION

Community Comparisons

For all subjects, lung function values, adjusted for measurable influences other than pollution exposure operating at the individual level, differed only slightly between communities with different levels or profiles of air pollution. When the subjects were divided by sex, the results showed statistically significant relationships between certain pollutant exposures and lung function losses, primarily in girls, which may have public health significance.

Available literature on differences between sexes in response to air pollution do not provide a clear picture. A study of the effects of ozone in German schoolchildren showed a more pronounced effect in boys (7) while a study in the Netherlands of traffic-related pollution showed stronger associations for girls (8). A previous study performed in Southern California found associations of lower lung function in females beginning at age 7. This was not seen in males until age 15, suggesting earlier effects in female subjects (9).

The data were adjusted for all factors known to affect pulmonary function, and we have not identified a confounder that would explain these relationships. Considering that the quality of data on pulmonary function could vary by community according to the level of exposure, we performed two tests of pulmonary function data quality. The first examined the mean differences of the best and next best test results for the four pulmonary function outcomes. These did not differ by community, nor were they correlated with level of pollution. The second looked at the proportion of expiratory efforts not accepted by the computer, by community. Again there were no significant associations with pollution level. There was a slight tendency for the data quality to be higher for the male subjects. The data quality do not vary significantly by age for either sex.

Girls spend less time outdoors and less time exercising than boys, which should result in less exposure to ambient pollution. In our data, the median outdoor time per week for girls in the 4th, 7th, and 10th grade was 10.0, 10.3, and 8.4 h and for boys was 10.3, 12.3, and 12.8 h. Our assessment of outdoor activity was based on an attempt to get "typical" activity. Since this information was collected over a 6-mo period, seasonal factors could add to the variability in response, although seasonal factors are less variable in Southern California than in most parts of the United States. Further, while intense midday heat during summer in our inland communities might result in decreased activity, the activity assessments were not conducted during summer.

There are several differences between sexes that could be playing a role, although the mechanisms by which they could be acting is not obvious. There is a difference between sexes in the relationship between volume and flows observed by Dockery and colleagues (10) and by Schwartz and associates (11). These differences could lead to a sex-related response to air pollutants. Another difference is the growth rate of adolescent boys and girls, with girls achieving their full height and maximum lung size considerably earlier. Whether the growth process affects response to air pollutants is not known. There are obvious differences between sexes in hormonal factors. Whether these differences affect defense mechanisms and/or response to air pollutants is not known. Differences in the response to cigarette smoking also have been observed, with larger effects seen in young women (12).

TABLE 4

REGRESSION OF PULMONARY FUNCTION TESTS (PFT) ON 1994 AMBIENT AIR POLLUTANTS*

PFT Pollutant[†]	Males				Females			
	Less Outdoors		More Outdoors		Less Outdoors		More Outdoors	
	B	SE	B	SE	B	SE	B	SE
FVC								
Peak O_3	182.7	(66.2)	−128.6	(56.0)[‡]	−119.6	(56.9)	79.6	(58.0)
PM_{10}	35.6	(68.2)	−32.9	(53.5)	−14.7	(53.6)	−73.9	(43.9)
$PM_{2.5}$	32.3	(75.3)	−24.5	(59.3)	−19.2	(58.8)	−80.7	(48.3)
NO_2	−5.3	(77.5)	−22.4	(60.6)	−19.7	(59.9)	−100.1	(45.8)
Acid	57.3	(53.2)	−54.4	(40.7)	−64.1	(38.7)	−26.4	(39.5)
FEV_1								
Peak O_3	148.9	(49.8)	−136.3	(51.3)[‡]	−89.8	(32.4)[‡]	−11.5	(34.8)
PM_{10}	37.9	(52.6)	−7.0	(52.7)	−24.7	(33.0)	−66.2	(18.0)[‖]
$PM_{2.5}$	46.6	(57.4)	−3.4	(58.0)	−26.3	(36.3)	−75.0	(18.8)[‖]
NO_2	38.6	(59.2)	−10.1	(59.1)	−17.8	(37.6)	−79.9	(17.8)[‖]
Acid	60.5	(39.4)	−56.7	(38.9)	−41.0	(24.3)	−45.1	(17.3)[‡]
PEFR								
Peak O_3	272.2	(153.5)	−71.0	(86.7)	−329.4	(92.4)[§]	−246.6	(78.1)[‡]
PM_{10}	42.6	(137.9)	54.0	(68.4)	−103.3	(104.6)	−159.2	(70.8)[‡]
$PM_{2.5}$	78.9	(150.1)	90.3	(72.0)	−125.9	(113.6)	−163.6	(80.2)
NO_2	118.4	(150.6)	55.9	(77.1)	−70.6	(120.7)	−140.8	(86.6)
Acid	162.7	(100.0)	−14.4	(57.1)	−143.4	(76.6)	−128.0	(57.8)
MMEF								
Peak O_3	176.4	(110.6)	−165.8	(92.7)	−154.1	(81.5)	−224.1	(57.7)[‖]
PM_{10}	−7.3	(97.4)	51.2	(82.2)	−118.3	(64.7)	−131.2	(63.5)
$PM_{2.5}$	28.9	(106.7)	67.3	(89.6)	−151.5	(66.9)[‡]	−152.6	(67.9)[‡]
NO_2	67.1	(107.1)	12.8	(93.8)	−111.7	(75.9)	−138.1	(72.9)
Acid	80.6	(74.9)	−65.6	(64.8)	−69.2	(56.6)	−132.2	(45.2)[‡]

For definition of abbreviations, *see* Table 1.

  * Single pollutant models adjusted for personal and environmental factors stratified by time outdoors. Models for all subjects are adjusted for the variables footnoted by [‡], [§], and [‖] in Table 3, the variables listed in the footnote of this table, height[2], weight[2], the two-way interaction of sex and grade with age, race, height, height[2], weight, and weight[2]. Models for females and males are adjusted for the same variables except those involving sex.

  [†] Regression coefficients are scaled to the interquartile range for each pollutant as follows: 40 ppb of O_3, 25 $\mu g/m^3$ of PM_{10}, 15 $\mu g/m^3$ of $PM_{2.5}$, 25 ppb of NO_2, and 1.7 ppb of acid ($HCl + HNO_3$, measured on a mole basis). Four models are fit for each pulmonary function test, one for each pollutant.

  [‡] $p < 0.05$.

  [§] $p < 0.01$.

  [‖] $p < 0.005$.

In addition, asthma prevalence rates vary between males and females by age. In the 4th graders, boys have a significantly higher rate, with the girls catching up by the 10th grade. This rising incidence in asthma in females may play some role in explaining the differential response to air pollution in female subjects.

The study was designed to have the optimal power for identifying and distinguishing specific pollutant effects, given the constraints of pollutant distributions in Southern California and budget limitations. The analysis presented here does not allow us to identify a specific pollutant responsible for the effect with any degree of certainty, although it seems likely that some combination of O_3, PM_{10}, and NO_2 is involved. For each of the four pulmonary function outcomes, a different pollutant was found to be the most strongly associated. Based on our knowledge of the potential chronic effects of the pollutants we were examining, we did not feel that we could reliably predict the pulmonary function end point most likely to be affected by a specific pollutant. Ozone, NO_2, and acid vapor as gaseous irritants might produce airway effects and/or inflammation, either of which could potentially result in obstructive effects (manifested by changes in MMEF) or parenchymal effects (manifested by changes in FVC). PM_{10} or $PM_{2.5}$ might be more likely to produce parenchymal effects than airway effects if deposition becomes significant, but there are also irritant components in the particles. We therefore have no pathophysiologic explanations for our findings.

The complex chemical reactions occurring in the atmosphere between the pollutants and the conversion of gaseous nitrogen compounds to nitrate particles add to the complexity of teasing out specific effects. The relatively high statistical correlation between some of the pollutants further complicates the isolation of effects attributable to one pollutant.

This study was designed to be a longitudinal study, with the hope that the cross-sectional data would provide useful results. The results presented here suggest an association between pollution levels and effects on pulmonary function in female subjects. Even though we have measures of physical size in these subjects, we do not know the rates of growth. On the assumption that the growth rate is an important determinant of both level of pulmonary function and the response to air pollution, we should be in a much better position to assess the pollutant–health effects issue with longitudinal data.

This study relies on air pollution measurements made at community monitoring stations. There are variations of ambient concentrations within communities over which we have no control. The information that we have on spatial and physical activity of our subjects is limited. We do know that schoolchildren are indoors 85% of the time or more. We have limited data on the exposures occurring in microenvironments common to the children in our study, i.e., homes and schools, which will be reported elsewhere.

In principle, our experimental design could not distinguish acute reversible effects of recent air pollution exposure from

| | Male | | | | Female | | | |
| | Asthmatic | | Nonasthmatic | | Asthmatic | | Nonasthmatic | |
	B	SE	B	SE	B	SE	B	SE
FVC								
O_3	94.4	49.0	35.1	27.8	−248.8[‡]	78.5	6.4	35.9
PM_{10}	−7.2	45.1	−7.3	−23.4	−38.4	86.7	−45.0	24.5
$PM_{2.5}$	7.4	49.6	−9.1	25.7	−52.6	94.7	−58.1[†]	25.1
NO_2	−5.2	50.6	−30.1	24.6	29.3	97.6	−74.2[‡]	21.3
Acid	30.2	35.4	−1.5	19.1	−64.3	68.1	−40.7	19.0
FEV₁								
O_3	107.4	69.5	40.0	23.4	−135.0[†]	57.2	−16.9	24.0
PM_{10}	25.4	60.3	2.4	20.9	−58.1	53.1	−41.7[†]	14.2
$PM_{2.5}$	30.5	66.2	4.2	22.9	−46.9	59.9	−51.3[§]	13.8
NO_2	29.2	67.6	−8.2	23.3	25.6	62.4	−55.5[§]	12.8
Acid	41.5	47.7	8.4	16.8	−26.1	44.9	−34.8[†]	11.2
PEFR								
O_3	614.1[‡]	189.8	47.5	67.8	−438.6	270.6	−144.3[†]	58.4
PM_{10}	192.7	204.9	−3.8	54.6	−444.6[†]	193.7	−130.4[†]	41.3
$PM_{2.5}$	231.3	223.2	5.7	60.0	−495.0[†]	211.3	−144.5[†]	45.0
NO_2	207.2	230.3	13.3	61.1	−393.6	237.5	−122.7[†]	52.6
Acid	283.0	148.7	27.7	43.5	−318.2	166.3	−95.3[†]	36.6
MMEF								
O_3	37.7	162.0	31.5	24.8	162.3	216.2	−129.6[†]	46.8
PM_{10}	38.0	127.3	24.8	19.5	−288.8	149.2	−99.7[†]	37.5
$PM_{2.5}$	9.0	140.5	37.6	19.8	−211.4	180.2	−132.7[§]	33.7
NO_2	35.8	142.8	25.1	22.2	−136.8	191.1	−121.6[†]	39.1
Acid	06.0	103.8	23.4	15.4	58.9	140.8	−85.0[†]	29.3

For definition of abbreviations, *see* Table 1.
* Adjusted for personal and environmental factors.
[†] $p < 0.05$.
[‡] $p < 0.01$.
[§] $p < 0.005$.

the chronic effects of interest. As mentioned previously, we minimized the possibility of acute effects by scheduling health testing to avoid hours or seasons with high O_3. A concurrent study evaluated elementary schoolchildren's acute effects in three communities with contrasting air quality, chosen to resemble three of our communities (13). It showed that morning FVC measurements decreased with increase in PM or NO_2, measured over the preceding 24 h. The acute effects were about 0.4 ml per parts per billion (ppb) of NO_2 in contrast to the chronic effect seen here of 1.7 ml/ppb.

The counterintuitive finding of significantly increased FEV_1 in active smokers requires explanation. At least part of the nonsmokers' function "deficit" may be real, assuming that subjects with initially poorer lung function were less likely to take up smoking, and that most of those who did smoke had not done so long enough to cause appreciable function loss. Previous evidence concerning effects of active smoking by young people is mixed but shows some consistency with those assumptions. Gold and coworkers (12), examining 10- to 18-yr-old subjects in the Six Cities Study, found higher FVC in smokers compared with nonsmokers, and similar or higher FEV_1, but lower MMEF and FEV_1/FVC ratios. Tager and colleagues (14) found generally lower FEV_1 in children and adolescents who smoke but little difference between nonsmokers and smokers with low total consumption. Beck and coworkers (15), comparing young smokers and nonsmokers, found higher FEV_1 in female smokers aged 7–14 and lower FEV_1 in their male counterparts, but the sex differences reversed in the 15–24 age range. Clear negative effects of smoking were seen in college students by Peters and Ferris (16).

Comparison with Previous Findings: Toxicology

Evidence from acute and chronic animal exposure studies and acute studies of human volunteers leaves little doubt that O_3 can cause unfavorable respiratory effects at exposure levels within or slightly above ambient range. This evidence has been reviewed recently (17–20). Multiple animal studies have shown apparently irreversible lung pathology, usually most evident in small peripheral airways, after several weeks to several months of intermittent exposures simulating diurnal variations of ambient O_3, with maximum concentrations of 200–250 ppb. Heavily exercising adult humans exposed in laboratories for periods of 6 hr or longer to O_3 concentrations as low as 80–120 ppb have shown acute lung dysfunction (21, 22) and lung inflammation (23). Dose–response relationships have been worked out in detail for lung dysfunction (24), and exposures to O_3 containing ambient pollution have been shown to evoke similar responses (25, 26). The acute effects are primarily restrictive rather than obstructive and may indicate an inability to take a full inspiration, but inflammatory responses are likely more important than acute lung dysfunction as precursors of chronic effects, and prolonged lung inflammation may lead to either restrictive or obstructive changes (19).

In contrast to O_3, NO_2 has shown no acute effects at ambient-like concentrations in some animal and human exposure studies, and relatively mild and subtle effects in others (20). Some investigators have reported small acute lung function losses and/or increased bronchial reactivity in volunteers with asthma exposed briefly to 500 ppb or less (27, 28), but the most extensive human exposure studies have not found such effects to be statistically significant, although in some instances a minority of subjects appeared to be reactive (29, 30). In any event, toxicologic evidence has demonstrated that NO_2 is generally less acutely toxic than O_3 at ambient concentrations.

Toxicologic assessment of PM_{10} effects is considerably more complicated. The composition of PM_{10} exhibits considerable geographic variation, even within Southern California, and actual ambient PM_{10} pollution is far more complex physically and chemically than particulate matter generated artificially for exposure studies. Many controlled exposure studies have employed sulfuric acid aerosol, which is suspected to be the most toxic component of PM_{10} in many locations but is not important in Southern California. Human studies have shown no more than small or equivocal respiratory effects of sulfuric acid, unless concentrations far exceed the ambient range (31–35). Prolonged repeated exposures to combined sulfuric acid and O_3 showed only marginally increased effects, as compared with O_3 alone (22). This finding might be relevant to the parts of Southern California where different strong acid—nitric acid vapor—may accompany O_3.

Comparison with Previous Findings: Epidemiology

The CORD studies, the only previous large-scale comparison of lung function across different parts of Southern California, suggested lower function levels and more rapid loss rates in adults living in more polluted communities (1). The most polluted CORD study sites were high in PM_{10} as well as O_3, so the observed effects might be attributed to either. Although not directly comparable because of subjects' age differences, the CORD findings appear consistent with our findings of an unfavorable long-term effect of O_3. Further support is provided by an analysis of data collected nationwide in the NHANES II survey, which suggested decreases in adults' lung function with increasing annual average O_3 concentration in their areas of residence (36). A preliminary evaluation of lung

function in U.S. Military Academy cadets in relation to long-term O_3 exposure (37) suggested effects on FEV_1.

We are not aware of prior epidemiologic studies that assessed effects of long-term NO_2 exposure on lung function. Multiple studies of symptom and illness rates in relation to indoor or outdoor NO_2 pollution have yielded mixed results (20).

The most directly relevant prior epidemiologic studies have been conducted away from Southern California and have been concerned primarily with particulate pollution. The Six Cities Study showed no significant association between recent or lifelong particulate exposure and FVC or FEV_1 (4, 38). All six cities were low in O_3 in comparison with our most polluted communities. In the subsequent 24 Cities Study, results show that bronchitic symptoms are again associated with particulate exposure (specifically, with the strong acid component) (39), and lung function is reduced in association with those exposures (40), in contrast with the Six Cities Study. The predicted loss due to lifelong residence in the community with the highest strong acid particulate concentration, relative to the cleanest community, was about 3% for FVC and FEV_1. Ozone effects were not reported. Most of the 24 cities had relatively little O_3 compared with our most polluted communities. In a study of preadolescent children in 10 rural Canadian communities, five of which had elevated O_3 and particulate sulfate, significant FVC and FEV_1 decrements between 1 and 2% were found in the five polluted communities (41). No significant excess respiratory morbidity was reported on questionnaires from the five polluted communities. Their annual mean of 1-h daily O_3 peaks was 46 ppb, less than half the value in our most polluted communities. Comparison of strong acid or particulate concentrations between studies is difficult because of differences in the atmospheres and in the measurement techniques.

We measured lung function in 3,293 Southern California public schoolchildren and adolescents. After appropriate adjustment for personal and household characteristics, statistically significant and perhaps physiologically important losses in FVC, FEV_1, PEFR, and MMEF were associated with pollution levels in females. The effects were larger in those females spending more time outdoors. Decreased FVC and FEV_1 were associated with peak O_3 exposure in male subjects spending more time outdoors. Given the inherent weaknesses of cross-sectional data, the follow-up of this cohort should provide valuable information on the relationships between air pollutants and lung development.

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