The Harvard Southern California Chronic Ozone Exposure Study: Assessing Ozone Exposure of Grade-School-Age Children in Two Southern California Communities

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The Harvard Southern California Chronic Ozone Exposure Study measured personal exposure to, and indoor and outdoor ozone concentrations of, approximately 200 elementary school children 6–12 years of age for 12 months (June 1995–May 1996). We selected two Southern California communities, Upland and several towns located in the San Bernardino mountains, because certain characteristics of those communities were believed to affect personal exposures. On 6 consecutive days during each study month, participant homes were monitored for indoor and outdoor ozone concentrations, and participating children wore a small passive ozone sampler to measure personal exposure. During each sampling period, the children recorded time–location–activity information in a diary. Ambient ozone concentration data were obtained from air quality monitoring stations in the study areas. We present ozone concentration data for the ozone season (June–September 1995 and May 1996) and the nonozone season (October 1995–April 1996). During the ozone season, outdoor and indoor concentrations and personal exposure averaged 48.2, 11.8, and 18.8 ppb in Upland and 60.1, 21.4, and 25.4 ppb in the mountain towns, respectively. During the nonozone season, outdoor and indoor concentrations and personal exposure averaged 21.1, 3.2, and 6.2 ppb in Upland, and 35.7, 2.8, and 5.7 ppb in the mountain towns, respectively. Personal exposure differed by community and sex, but not by age group. *Key words*: children, chronic, exposure, ozone, personal, sampler, Southern California. *Environ Health Perspect* 108:265–270 (2000). [Online 4 February 2000]
http://ehpnet1.niehs.nih.gov/docs/2000/108p265-270geyh/abstract.html

Almost three decades ago, in response to the Clean Air Act of 1970, the U.S. Environmental Protection Agency promulgated National Ambient Air Quality Standards (NAAQS) (*1*) for six air pollutants: ozone, total suspended particles, nitrogen dioxide, sulfur dioxide, carbon monoxide, and lead. At that time, it was generally believed that only residents of Southern California were at risk for exposure to high ozone concentrations. Now almost every statistical metropolitan area in the United States has reported violations of the 1979 ozone standards of 0.12 ppm for 1 hr during a single year. In 1995, 50 cities across the United States exceeded the air quality standard one or more times (*2*). In 1997, the NAAQS for ozone was changed to an 8-hr integrated value of 0.08 ppm. Compliance will be based on 3 years of monitoring, where the fourth highest 8-hr average in a calendar year cannot exceed 0.08 ppm. Analysis in anticipation of the new standard indicates that even more Americans will be living in areas that exceed healthy levels (*3*).

Chamber studies and other acute exposure studies suggest that short-term effects of ozone on respiratory function and sensory irritation are reversible. However, only a few investigations have studied the chronic effects of ozone exposures over months and years. Using ambient ozone data collected from local monitoring sites, Schwartz et al. (*4*) reported highly significant ozone-associated reductions in lung function for people living in areas where annual ozone concentrations exceeded 40 ppb. Time–series analysis of daily mortality in Los Angeles showed an association with ozone concentration that was significant for both respiratory and cardiovascular-related deaths (*5*). Further, the work of Burnett et al. (*6*) in Ontario, Thurston et al. (*7*) in New York (*7*), and White et al. (*8*) in Atlanta are consistent in showing an association among contemporary measures of ambient ozone and hospital admissions, particularly for asthma.

Although these studies suggest a chronic effect for ozone, they are still limited by a lack of understanding of the relationship between ambient measurements and personal exposures. Several questions about chronic ozone exposure remain unanswered. The relationship between ambient ozone and personal exposures of individuals living in a community has not been adequately addressed, and the interpersonal variability in ozone exposures that are expected because of behavior, housing characteristics, and spatial differences in ozone concentrations has not yet been quantified.

Until recently, collecting personal ozone exposure information has been difficult. Only ultraviolet (UV) photometric or chemiluminescence continuous ozone monitors have been available for ozone concentration measurements and they are too heavy and cumbersome to be carried around by individuals for personal monitoring purposes. Small lightweight passive ozone exposure monitors, however, are now available. These monitors make personal and microenvironmental monitoring feasible (*9–11*). The Harvard passive ozone sampler is one such device that depends on the reaction between ozone and the nitrite ion for ozone concentration measurement (*11*). Over the last several years, short-term personal ozone exposure studies have been carried out by several researchers using this monitor (*12–15*). These studies demonstrated the feasibility of monitoring personal exposure of both children and adults for periods of up to 1 week.

The purpose of this study was to profile personal exposure to ozone over a time period that would provide information for the discussion of potential chronic effects of exposure to ozone. Data obtained from this work will be used to develop a model for estimating annual personal ozone exposure. The study was designed to measure exposure over a time period that would capture seasonal variations in ambient ozone concentrations and in locations which would demonstrate the impact of geographical location on exposure. The Harvard Southern California Chronic Ozone Exposure Study measured personal exposure to, and the indoor and outdoor ozone concentrations of, elementary school children for 12 months (June 1995–May 1996). Two

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We thank A. Fox, L. Sanchez, C. Bench, L. Kole, N. Scopen, M. Simun, M. Palmer-Rhea, D. Belliveau, D. Burlow, and J. Arnold. We also thank the University of Southern California Department of Preventive Medicine. Most importantly we thank the children and their families for their participation and hard work; without them this study could not have succeeded.

This work was supported by National Institute of Environmental Health Sciences grant R01-ES06370 at the Harvard School of Public Health.

Received 11 May 1999; accepted 21 September 1999.

communities were selected because of certain characteristics that were believed to affect personal exposures. Neither of the communities was in compliance with the NAAQS for ozone. In this first paper from the study, we present the study methods and descriptive results. Annual and monthly ozone personal exposures are examined within and between communities. Age, sex, housing, and community factors that could potentially impact personal exposures are also presented to derive a first level of understanding of the variables that could be important in subsequent modeling efforts.

Methods

The communities selected for the study were Upland and several neighboring mountain towns in San Bernardino County, California. San Bernardino County is on the eastern edge of the Los Angeles air basin. Upland, elevation approximately 0.15 km above sea level and 80.5 km east of Los Angeles, was chosen as representative of Southern California communities with moderate to high ambient ozone levels. The mountain towns are approximately 50 km further east of Upland and were selected because they experience some of the highest ambient ozone concentrations in the country. The mountain towns are located between 1.2 km (Crestline) and 1.8 km (Running Springs) above sea level. Community selection decisions were based on 1994 ambient ozone data, which showed that the mountain locations experienced consistently higher ozone concentrations than Upland (*16*). Both communities have a distinct annual ozone distribution, with the summer months typically 2.5 times the winter month averages.

Study design. Children were recruited from elementary schools. After a presentation at their school, the children were recruited for participation by a questionnaire and a letter to their parents. Approximately 4,300 children were contacted. Of these, 634 returned questionnaires with a positive response to study participation. From this group, 224 children from 156 homes were selected. These children were in grades 1–5. The cohort was not intended to be a random sample. Because the study period was 12 months, children who were more likely to complete the study were chosen. Children were selected if they responded enthusiastically with additional comments on their questionnaire and/or if the parents requested participation. For purposes of a parallel study involving preschool-aged children, children were selected if they had siblings 4 years of age or younger. Most respondents indicated that they had gas appliances. To investigate the effect of cooking fuel type on exposure, children were preferentially selected if their home had an electric cooking range (80% had gas and 20% had electric). Selection on the basis of home air conditioning (AC) was not possible. Of the mountain homes, only 1.7% had AC, whereas 93% of the homes in Upland had AC. The initial cohort included 119 females and 105 males.

Personal, indoor, and, outdoor ozone concentrations were measured each month for 12 months starting 7 June 1995 and ending 29 May 1996. Personal samplers were worn on the chest, clipped directly to outer clothing, for 6 consecutive days each month. Samplers were worn continuously, except when the participant was sleeping, bathing, swimming, or engaged in an activity such as soccer, for which wearing the sampler was not allowed. During these times they were placed nearby in an open area. Indoor and outdoor ozone concentrations at participants' homes were monitored using passive ozone samplers. Indoor samplers were clipped to stands supporting small fans and were placed upwind of the fans, which provided constant air flow across the collection face of the sampler. Samplers were installed in the room where the family reported spending a large part of their time at home. Fan stands were placed on bookshelves or tabletops, situated so that the fan was drawing air from the center of the room; we avoided placing fan stands opposite of frequently opened windows and doors, working fireplaces, or ceiling fans. Outdoor samplers were located in the back of homes in an open area not covered by a tree canopy or roof overhangs. Samplers were placed at least 2 m off the ground, usually attached to deck railings or fence posts, and always protected by a polyurethane cap.

Each month the participating children wore a passive ozone sampler for 6 consecutive days (approximately 144 hr) and recorded their activities on a structured diary form. During the same 6 days, indoor and outdoor samplers were placed at their homes. Diaries were divided into 30-min increments across a 24-hr time period (the increment from 0000–0600 hours was 1 hr). A child was given one diary page for each day of sampling. The diary was divided into four categories: indoor, outdoor, travel, and activity. The children were asked to indicate whether they were at home, school, some other place, or traveling under the location categories. They gave a brief description of the actual activity for each time period, e.g., playing basketball, studying, or eating in a restaurant, and estimated travel time under the activity category.

The study population in each community was divided into four cohorts. Each cohort was monitored once each month; therefore, monitoring all of the children in each community required 4 weeks. The order in which the four cohorts were monitored throughout the month remained the same for the entire study year. During each study week, sampling began on Wednesday and concluded the following Tuesday. Field technicians visited homes during times when the children were present. The children were given a sampler to wear and a time activity diary to record their 30-min activities. At each home, personal, indoor, and outdoor samplers were deployed within approximately 5 min of each other. The field technician returned 6 days later to collect the samplers and review the diaries with the child and the parent.

We conducted sampling during 46 of the 48 weeks in the study year. No sampling was carried out during the first week of June 1995, when staff members were confirming participation with study families, and during the 1995 Christmas holiday week.

We encouraged participation with $50 savings bonds awarded at the end of 6, 9, and 12 months. At the beginning of the 1995–1996 school year, the effort of the participating children was acknowledged at school assemblies, where they were presented with study tee shirts. Children who completed at least 10 months of the study were awarded certificates of completion. During the study year, the field staff rewarded children with small homemade treats and demonstrated appreciation for hard work by attending birthday parties, soccer games, and school events.

Each week, approximately 15% of all samplers used in the field were set aside as field blanks. Blanks were handled by exposing them briefly to indoor air, returning them to their plastic bag and amber canister, and then leaving them at room temperature during the 6 sample days at a field technician's home. In addition, approximately 15% of all samplers each week were divided equally between indoor, outdoor, and personal exposures, and were exposed as duplicates.

Sampling method. Continuous ambient ozone measurements were obtained from two monitoring stations operated by the South Coast Air Quality Management District in Diamond Bar, California. These stations are in Upland and Crestline, one of the mountain communities. The Upland station is in a trailer park on the eastern edge of the town, approximately 2 km from the San Bernardino Freeway. The Crestline station is on the shore of Lake Gregory, a recreational lake approximately 1.2 km above sea level. The UV photometric ozone analyzers (Dasibi 1008-RS; Dasibi Environmental Corporation, Glendale, CA) used have a 1-ppb limit of detection (LOD).

Integrated personal, indoor, and outdoor ozone measurements were made using the

Harvard passive ozone sampler (*11*). All samplers were prepared at the Harvard School of Public Health (HSPH; Boston, MA) 1 week before deployment in the field. For shipping, samplers were sealed in resealable plastic bags, then placed in amber canisters. The samplers were shipped cooled to California by overnight delivery and used in the field the next day. At the end of the sampling period, the samplers were retrieved, stored in refrigerators, and then returned to HSPH in cold containers by overnight delivery. The samplers were refrigerated until they were analyzed. All of the samplers were analyzed between 1 and 3 weeks after returning to the HSPH.

Harvard passive ozone sampler. The Harvard passive ozone sampler is composed of a Teflon barrel containing two glass fiber filters, one at each end of the barrel (Ogawa and Co. USA, Inc. Pompano Beach, FL), as shown in Figure 1. The filters were coated with a previously described nitrite-containing solution (*11*). They were held in place by perforated endcaps that act as diffusion barriers. To deploy the sampler, the barrel was attached to a plastic badge equipped with a metal clip. The clip was used to secure the sampler to the sampling location.

The sampler collects ozone using the oxidation reaction of nitrite by O_3 to form nitrate. The average ozone concentration measured by the sampler was calculated from amount of NO_3^- accumulated, which was determined by ion chromatography (Dionex model 2000i; Dionex Corporation, Sunnyvale, CA), and the appropriate effective collection rate (ECR). Ozone concentrations were calculated as follows:

$$C_{O_3} = \frac{N \times V \times MW_{O_3} / MW_{NO_3} \times R}{ECR \times K \times MW_{O_3} \times T} \quad [1]$$

where C_{O_3} is the integrated ozone concentration in parts per billion; N is the corrected nitrate concentration (sample minus average blank, in milligrams per milliliter); V is the extraction volume in milliliters, 5 mL; MW_{O3} and MW_{NO3} are the molecular weights of ozone and the nitrate ion, respectively, in milligrams per micromole; R is the conversion factor 106 in cubic centimeters per cubic meter; ECR is the effective collection rate in cubic centimeters per minute; K is the conversion constant 0.0409 mg/(ppb/m^3) determined at 298 K and 1 atm; and T is the exposure time in minutes.

Interferences. Interferences from other pollutants are a potential concern with the chemistry of this method. Possible interferences include NO_2, HONO, PAN, H_2O_2, and SO_2, and interference testing was carried out in the environmental exposure chamber at the University of California, Riverside. When passive samplers were exposed to high concentrations of these potentially interfering species for relatively long time periods, researchers at the University of California, Riverside, found little interference from NO_2, HONO, PAN, and SO_2. The researchers found significant interference from H_2O_2 in the high-concentration range; however, the effect under ambient conditions is likely to be negligible. HNO_3, which is expected to present a positive interference, was not tested because of the difficulty of generating a stable nitric acid atmosphere. However, at concentrations typical of those found in Southern California, the interference for this method would be approximately 5% of measured ozone (*17*).

ECR. The theoretical ECR for the passive sampler is 21.8 cm^3/min. Under constant wind conditions, sampler performance is not affected by the large changes in temperature or relative humidity in ambient air and typical of residential locations. The precision of the passive sampler is approximately 10% over a wide range of concentrations. However, wind tunnel tests show that the collection rate of the sampler is significantly affected by variations in face velocity (*18*).

For outdoor sampling, we solved the effect of varying face velocity by using a protective cap. Use of the protective caps with this sampler in different studies gave an ECR close to theoretical: 21.6 cm^3/min (*19,20*). The ECR used in this study for determining outdoor ozone concentrations was also 21.6 cm^3/min.

It was important to ensure sufficient air movement across the face of the passive sampler for indoor air sampling. To control the face velocity for indoor sampling, we placed the sampler upstream of a small fan on a stand. The fan stand consisted of a small box fan supported by a lightweight metal frame. The passive ozone sampler was attached to the fan stand so that the sampling faces were parallel to the air flow. This method was similar to the timed exposure diffusion sampler (TEDS) used by the California Air Board in a Los Angeles study (*17*), but was less complicated and costly. Because face velocities for the indoor sampler were similar to those of the TEDS, which have an ECR of 21.3 cm^3/min, the same ECR was used to determine indoor ozone concentrations for this study.

The ECR used for personal sampling was determined from a controlled chamber experiment. To determine the collection rate of personal sampling, Liu et al. (*13*) studied five adult subjects who wore four passive samplers at different body locations while sitting in an exposure chamber. Using ozone concentrations measured in the chamber by continuous UV photometric ozone monitors, the ECRs for passive samplers at each body location were determined; they ranged from 17.7 ± 2.3 to 10.3 ± 2.9 cm^3/min. The mean ECR for samplers at all body locations was 14.8 ± 2.9 cm^3/min, which we used in this study.

Quality assurance. Ozone concentrations were calculated according to Equation 1. Background blank values, determined from week-specific field blanks, were subtracted from the sample nitrate measurements. The LOD was determined at 3 SDs of the average nitrate concentration from field blanks. The LOD based on a 144-hr exposure was 1.0 ± 0.57 ppb, with the weekly LODs ranging from 0.3 to 2.8 ppb. LODs for this study corresponded to the range reported by others [0.5–2.0 ppb; (*13,14,21*)].

Precision was determined from 602 duplicate comparisons. Figure 2 shows a comparison of the duplicate samples and the overall correlation coefficient (r^2 =0.95). We calculated precision by the root mean square estimate method and reported it as a percentage. The precision was 9% for personal (n = 158), 12% for indoor (n = 239), and 4% for outdoor (n = 205) samplers. The

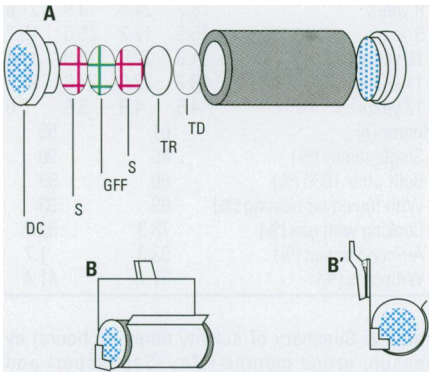

Figure 1. (*A*) Configuration of the Harvard passive ozone sampler. Abbreviations: DC, diffusion cap; GFF, coated glass fiber filter; S, screens that support the coated glass fiber filter; TR and TD, Teflon supports for the screens and filter, respectively. (*B*) Front view of the assembled badge. (*B'*) Side view of the assembled badge.

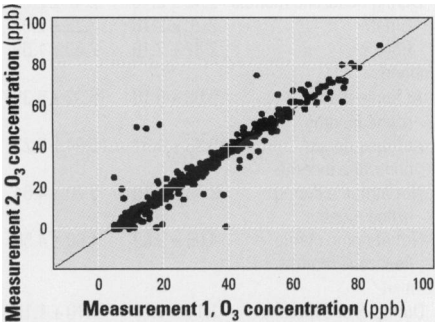

Figure 2. Comparison of the duplicate samples and the overall correlation coefficient. Slope = 0.99, intercept = 0.42, r^2 = 0.95, n = 602.

percentage of all samplers that fell below the LOD was 10.4% (6.1% personal, 19.7% indoor, and 0.05% outdoor). We used a value of 50% of the LOD, or 0.5 ppb, for the following analyses.

From June to August 1996, 30 triplicate sets of passive samplers were placed at the local monitoring stations. The sampling period was 144–168 hr. The mean passive sampler concentrations for each sampling period showed excellent agreement with the time-averaged hourly ozone concentrations, with an overall bias of + 3% and an $r^2 = 0.995$.

Statistical analysis. Statistical analyses of the data included simple least squares regression to estimate bias and the direction of the bias. Associated correlation coefficients were also determined. We used the *t*-statistic to test for differences in sample means. We assumed that the sample distributions were approximately normal, with missing values randomly distributed across seasons, sex, and location.

Table 1. Characteristics for children participating in the study for at least 6 months.

Characteristic	Upland		Mountain	
	Boys	Girls	Boys	Girls
Number of subjects	40	44	34	51
Participants by age (%)				
6 years	2.3	0.0	2.8	2.0
7 years	9.1	14.6	11.1	15.7
8 years	18.2	24.4	13.9	21.6
9 years	15.9	12.2	25.0	15.7
10 years	31.8	22.0	13.9	11.8
11 years	18.2	22.0	27.8	33.3
12 years	4.5	4.9	5.6	0.0
Homes (*n*)	61		55	
Single family (%)	85		98	
Built after 1960 (%)	80		83	
With forced air heating (%)	89		93	
Cooking with gas (%)	78.3		82.8	
Air-conditioned (%)	93.3		1.7	
With pets (%)	37.7		41.4	

Table 2. Summary of activity times (in hours) by season: ozone months (May–September) and nonozone months (October–April).

Average daily time	Upland[a] (mean ± SD)	Mountain[b] (mean ± SD)
Outdoors		
During ozone months	3.47 ± 2.70	3.88 ± 3.15
Girls	3.21 ± 2.67	3.65 ± 3.23
Boys	3.78 ± 2.72	4.16 ± 3.11
During nonozone months	2.49 ± 2.18	2.42 ± 2.04
Girls	2.20 ± 2.16	2.22 ± 2.03
Boys	2.87 ± 2.18	2.69 ± 1.69
Indoors		
At home during ozone months	15.69 ± 5.10	15.32 ± 5.35
At home during nonozone months	16.53 ± 4.51	15.94 ± 5.23
Not at home during ozone months	3.73 ± 4.19	3.70 ± 4.64
Not at home during nonozone months	4.06 ± 3.89	4.60 ± 4.58
Transit		
During ozone months	1.11 ± 1.17	1.10 ± 1.15
During nonozone months	0.91 ± 1.01	1.05 ± 1.09

[a]Number of daily diaries = 5,325. [b]Number of daily diaries = 5,004.

Results

During the yearlong study, 25% of the study subjects did not meet the minimum requirement of at least six sampling periods of valid measurements and completed forms. Most of the children who dropped out (28 of 40) left in the first half of the study. One hundred eighty-four children completed the study, but of those, 15 lacked housing characterization questionnaires. For a variety of reasons, obtaining housing characteristics information from these 15 households proved problematic for the field staff, who ultimately failed to secure completed questionnaires from this group. Data from 169 children were used in the analysis. These children lived in 116 homes, of which 61 were in Upland and 54 were in the mountain communities.

The average number of measurements per child across the study year, 10.7 ± 0.3, was independent of sex, age, or location. We found a similar result by season. Upland children averaged 4.4 ± 0.8 measurements during the ozone months (May–September) and 5.7 ± 1.1 measurements during the nonozone months (October–April), whereas mountain children averaged 4.6 ± 0.8 (ozone months) and 6.3 ± 1.2 (nonozone months) measurements.

Table 1 provides a summary description of the study population. Several housing factors are noted. During the ozone months, children living in the mountains were outdoors longer than children from Upland. Boys in both communities spent on average 30 min longer outdoors than girls. During the nonozone months, children spent on average 1 hr less outdoors than they did during the ozone months. Table 2 summarizes features of the children's diaries.

Table 3 summarizes the seasonal averaged ozone concentrations for outdoor, indoor, and personal passive sampling.

Outdoor. Average monthly ozone concentrations from all homes and from each central site monitoring station are shown in Figure 3. Outdoor monthly concentrations were derived from the average of all outdoor passive measurements collected over all four sampling periods each month at participant homes in each community. The average monthly ambient central site concentration for each location was determined from data retrieved from the Aerometric Information Retrieval System (*22*). The seasonal pattern of ozone in Southern California is evident and is consistent with historical data. Although there is spatial variability within each community, the Mountain–Upland differences persist.

In Upland, monthly averages of the outdoor home ozone concentrations were approximately 13% higher that the Upland monitoring station measurements ($r = 0.99$). The average of the home outdoor concentrations was consistently higher than the monitoring station throughout the study year. In the mountains, monthly averages of the outdoor home concentrations during the ozone months were approximately 4% lower as compared to central monitoring station average monthly measurements. However, during the nonozone months the relationship between the monthly outdoor home and ambient concentrations was similar to that in Upland, with the home outdoor measurements on

Table 3. Descriptive statistic of seasonal integrated outdoor and indoor ozone concentrations and personal ozone exposure levels divided by community.

Statistic	June–September 1995 and May 1996		October 1995–April 1996	
	Upland	Mountain	Upland	Mountain
Outdoor (ppb)				
Samples (*n*)	383	403	530	570
Mean	48.2	60.1	21.1	35.7
Median	47.6	57.6	19.3	35.8
SD	12.2	17.1	10.7	9.3
Minimum	9.1	3.9	0.5	13.6
Maximum	82.5	160.1	64.8	65.6
Indoor (ppb)				
Samples (*n*)	386	412	531	569
Mean	11.8	21.4	3.2	2.8
Median	9.5	19.7	1.5	0.6
SD	9.2	14.8	3.9	4.2
Minimum	0.5	0.5	0.5	0.5
Maximum	41.6	67.8	34.9	29.5
Personal (ppb)				
Samples (*n*)	345	367	479	520
Mean	18.8	25.4	6.2	5.7
Median	17.6	24.0	4.7	4.2
SD	10.1	13.4	5.4	5.1
Minimum	0.5	0.5	0.5	0.5
Maximum	62.6	72.3	40.7	31.2

average 15% higher than measurements made at the mountain monitoring station.

Outdoor home ozone concentrations in the mountain communities were higher than those found in Upland. During the high-ozone months, mountain concentrations were on average 20% higher than in Upland (two-tailed t-test, $p < 0.01$). During the nonozone months, concentrations in the mountains were on average 60% higher (two-tailed t-test, $p < 0.0001$).

Indoor. During the ozone months, average weekly indoor home concentrations in the mountain homes were almost 2 times those found in Upland (two-tailed t-test, $p < 0.01$). During the nonozone months there was no difference between the two communities (two-tailed t-test, $p > 0.05$). Figure 4 shows average monthly indoor concentrations across the entire study year for both communities.

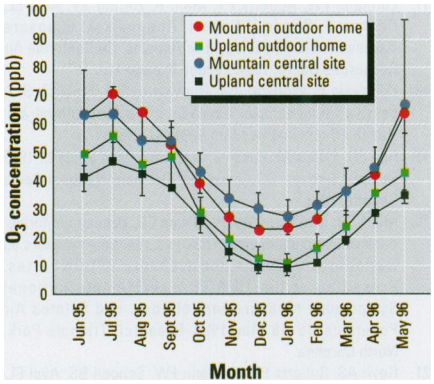

Figure 3. Ambient monthly ozone concentrations at central sites and across homes (SD) in each community.

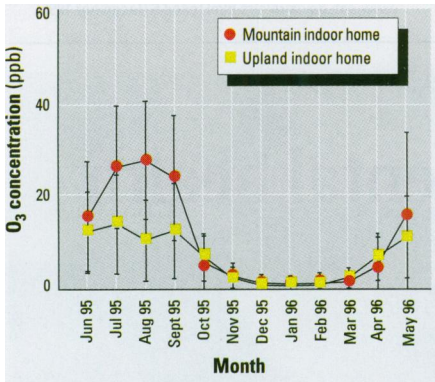

Figure 4. Indoor monthly ozone concentrations across homes (SD) in each community.

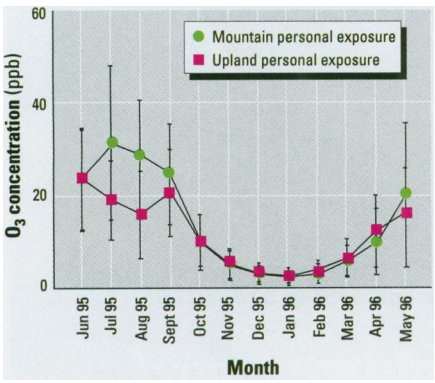

Figure 5. Personal monthly ozone concentrations across homes (SD) in each community.

Personal. During the ozone months, monthly average personal exposure measurements differed by community as well. Mountain community participants were exposed to, on average, 35% (two-tailed t-test, $p < 0.01$) more ozone than participants in Upland. In the nonozone months, there was no significant difference in average exposure (two-tailed t-test, $p > 0.05$). Figure 5 shows the average monthly personal concentrations across the entire study year in both communities.

Although there were differences among the four cohort groups within a month or season, the overall annual personal exposure concentrations were not significantly different. There were differences in exposure based on sex. Boys had higher personal exposures than girls independent of location of their homes or housing factors. Table 4 shows that this difference was larger when considering just the summer months.

Discussion and Conclusions

This study represents the first longitudinal estimation of exposure to ozone over a 1-year period. Personal, indoor, and outdoor ozone measurements were successfully collected for 184 children across a 12-month period in two high-ozone communities in Southern California. In addition to wearing a personal sampler for 6 consecutive days each month, the children recorded their activities during each day the sampler was worn. We collected information characterizing the home of each participant. Of the 184 children who completed the study, results from 169 were used in the analyses. We compared differences in ozone levels and exposure between communities in each season by outdoor and indoor ozone concentrations and by personal exposure. Personal exposure was evaluated between communities by sex and age.

The two communities were selected because of a large between-community difference in ambient ozone levels. Average monthly outdoor ozone concentrations measured at subject homes reflected the concentration trends reported by the local monitoring stations. The difference in ambient concentrations between communities was captured by the home outdoor measurements. In the mountains, winter concentrations remained approximately twice as high as those in Upland; monthly concentrations did not fall below 34 ppb. Spatial variation in ozone concentration across communities was reflected in the difference between the average of the home concentrations and the average ozone concentrations measured at the single-location monitoring stations. In Upland the difference between home outdoor and stationary site measurements across the study year was on average +13%. This may be a reflection of the fact that the majority of study homes were up slope and farther away from a major freeway than was the monitoring station. The difference between home outdoor measurements and stationary site measurements in the mountains varied with season. The average difference during the ozone months was -4%, whereas during the nonozone months the average difference was +15%. This difference may be an indication that the Crestline station, which was used for the mountain communities, was not a good indicator of ambient concentration for all of the mountain communities. The station was approximately 0.30 km below and 11.3 km west of Running Spring, where 24% of the participants lived.

Differences between communities were also reflected in indoor concentrations. During the ozone season, average indoor concentrations in the mountain homes were 3–17 ppb higher than in the Upland homes. This difference was due not only to higher ambient concentrations in the mountain communities, but also to differences in the way homes were ventilated. All but one of the mountain homes were ventilated by open windows, whereas all homes but six in Upland were air conditioned. As ambient levels decreased in the nonozone season months, the individual characteristics of homes influencing indoor ozone concentrations became less important. Although outdoor concentrations were higher in the mountains during these months, temperatures

Table 4. Comparison of personal exposure by sex and season.

	June–September 1995 and May 1996				October 1995–April 1996			
	Upland		Mountain		Upland		Mountain	
Personal exposure	Boy	Girl	Boy	Girl	Boy	Girl	Boy	Girl
Samples (n)	40	44	34	51	40	44	34	51
Mean	19.7	18.2	26.6	22.8	6.9	6.0	6.9	4.8
SD	7.8	6.5	8.7	9.3	2.8	2.9	3.3	2.1
Minimum	4.3	7.0	10.0	7.4	1.5	0.8	1.2	0.9
Maximum	39.4	35.2	48.9	49.7	12.6	14.9	17.9	10.5

were considerably lower in both communities and windows were kept closed. During the nonozone months there was essentially no difference in indoor concentration between the two communities.

Personal exposure also differed between communities during the ozone months. In the mountain communities, personal exposures were 0–12 ppb higher than in Upland, whereas during the nonozone months there was no difference in exposures between the two communities. In both communities boys' exposure was higher on average than girls', with boys and girls in the mountain communities experiencing higher exposures than boys and girls in Upland. We found no difference in exposure between the age groups that we investigated. This may be because children in elementary school are engaged in similar activities and have similar schedules during the school year.

Studies of chronic effects due to ozone exposure have been limited by lack of knowledge about personal exposure. The Southern California Chronic Ozone Exposure study provides personal exposure data across a time period that is relevant for understanding chronic effects and in geographical areas differing in ambient ozone concentrations. Current work is focused on developing models to estimate individual and community ozone exposure. The extent to which information about individual activities, time spent in different locations, and characteristics of participants' homes can be used to estimate exposure levels is being explored. Valid exposure models will yield estimates of ozone exposure in communities where no actual personal data are available, thus providing information for future epidemiologic studies.

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Ozone Exposure Assessment in a Southern California Community

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An ozone exposure assessment study was conducted in a Southern California community. The Harvard ozone passive sampler was used to monitor cohorts of 22 and 18 subjects for 8 weeks during the spring and fall of 1994, respectively. Ozone exposure variables included 12-hr personal O_3 measurements, stationary outdoor O_3 measurements from a continuous UV photometer and from 12-hr Harvard active monitors, and time–activity information. Results showed that personal O_3 exposure levels averaged one-fourth of outdoor stationary O_3 levels, attributable to high percentages of time spent indoors. Personal O_3 levels were not predicted well by outdoor measurements. A random-effect general linear model analysis indicated that variance in personal exposure measurements was largely accounted for by random error (59–82%), followed by inter-subject (9–18%) and between-day (9–23%) random effects. The microenvironmental model performs differently by season, with the regression model for spring cohorts exhibiting two times the R^2 of the fall cohorts (R^2 = 0.21 vs. 0.09). When distance from the stationary monitoring site, elevation, and traffic are taken into account in the microenvironmental models, the adjusted R^2 increased almost twofold for the fall personal exposure data. The low predictive power is due primarily to the apparent spatial variation of outdoor O_3 and errors in O_3 measurements and in time–activity records (particularly in recording the use of air conditioning). This study highlights the magnitude of O_3 exposure misclassification in epidemiological settings and proposes an approach to reduce exposure uncertainties in assessing air pollution health effects. *Key words*: active sampler, exposure assessment, ozone, passive sampler, time–activity pattern. *Environ Health Perspect* 105:58–65 (1997)

The current National Ambient Air Quality Standard (NAAQS) for ozone (O_3), 0.12 ppm, is based on the health effects due to acute exposures of 1 hr as measured by continuous monitors. However, exposures to O_3 for up to 8 hr at less than 0.12 ppm have been shown to result in progressive and significant changes in respiratory function in exercising individuals (*1–3*), suggesting that the current O_3 standard may not sufficiently protect public health. In response, one of the alternative O_3 standards being considered by the EPA is the 8-hr average concentration (*4*). The use of the integrated passive monitor to obtain exposures greater than 1 hr can greatly enhance our ability to determine the dose–response relationship for acute exposures to O_3. The 12-hr O_3 measurements are biologically significant when combined with the retention factor of O_3 in the deep lung and the ventilation rate to produce the 12-hr delivery dose of O_3 (*5*). Our recent epidemiologic study showed that these O_3 dose estimates, not 1-hr maximum O_3 measures at the stationary site, were associated with respiratory symptoms and inhaler use among asthmatics (*5*). Using the 12-hr personal measurements significantly reduces the magnitude of expected exposure misclassification in studies that have relied solely upon O_3 measurements from outdoor stationary site monitors to represent personal exposure to O_3.

Previous studies (*6–9*) that examined short-term (12-hr) personal O_3 exposures have involved relatively short monitoring periods, generally less than 5 days, or monitored less than five subjects simultaneously. Epidemiological research on the acute and adverse respiratory effects of O_3, on the other hand, generally involves repeated daily measurements over several weeks or months in larger cohorts (panel studies). To examine personal O_3 exposure and its determinants in a setting directly relevant to epidemiological research, the present exposure assessment study was integrated into two consecutive asthma panel studies. More precisely, this study involved daytime (12-hr) personal O_3 monitoring in cohorts of 23 and 18 subjects for two 8-week periods during the spring and fall of 1994, respectively. Extensive outdoor active monitoring throughout the study region was conducted during the fall period. Because of the diverse geographical characteristics of the study area, it was possible to examine variations of O_3 concentrations in a three-dimensional domain.

The purpose of this study was to investigate personal O_3 exposures among subjects during both spring and fall seasons in the Alpine area and to investigate the feasibility of using ambient O_3 measurements from one outdoor fixed site as well as the activity patterns from the subjects to predict personal O_3 exposures. This study further examined the influence of outdoor temperature on activity patterns and the effects of activity patterns on personal O_3 exposure levels. In addition, the extent of the effects of outdoor O_3 spatial variation on the predictive power of personal exposure models was investigated.

Methods

This study was conducted in the Alpine area of San Diego county, California. Alpine (population ~12,000) is located approximately 20 miles east of San Diego. Residents of the Alpine community live around or above the base of the average air inversion layer (1,200 ft or 366 m above sea level) (*10*). High levels of O_3 above 120 ppb have been measured on many days per year and a permanent government monitoring site (using a continuous UV photometric O_3 analyzer) has been in operation since 1981.

The Harvard O_3 passive sampler was used for personal monitoring. The principle of the sampler is oxidation of nitrite (NO_2^-) by O_3 to form nitrate (NO_3^-), which is quantified by ion chromatography (*11*). Field blanks (n = 184) and duplicate samples (n = 52) were used for quality assurance and quality control (QA/QC). The limit of detection (LOD), calculated as three times the standard deviation of the field blank values, was 17 ppb of O_3 for the 12-hr average samples. The uncertainty, defined as the variance of difference between duplicates divided by $\sqrt{2}$ (*12*), was 3 ppb.

Subjects recruited for the spring study included 9 males (mean age = 18 years; range = 10–38) and 13 females (mean age = 24 years; range = 10–47). Of these subjects, 13 were pediatric subjects and 9 were adults. Informed consent was obtained from all subjects who were monitored simultaneously from 9 May to 3 July 1994. During the fall, 18 subjects were monitored simultaneously from 6 September to 31 October 1994. These subjects included 11 males (mean age = 16 years; range = 9–38) and 7

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This study was supported by the National Institutes of Health, NIEHS grant ES06214.

Received 19 April 1996; accepted 18 September 1996.

females (mean age = 21 years; range = 9–38). Of these, 13 were pediatric subjects and 5 were adults. Fourteen subjects had been previously monitored in the spring. The monitoring duration was approximately 12 hr, starting when subjects awoke, generally between 6 and 8 A.M. Subjects were given clock-shaped time–activity diary forms to record activities (time indoors and outdoors, in Alpine area or outside Alpine area), the level of physical activities, and the use of air conditioning. The time resolution of the diary is 15 min.

The study area is located in a complex terrain, with an altitude ranging from less than 600 ft in the west to over 2,000 ft in the northeast (Fig. 1). During the fall study, in addition to the San Diego County Air Pollution Control District (APCD) monitoring sites at Alpine and El Cajon (west of Alpine), the Harvard O_3 active monitor (*13*) was used at 12 other outdoor locations chosen on the basis of providing a representative range of traffic volume and elevation in the community (Table 1). Passive samplers were collocated with four active monitors. The monitoring duration for the active samplers was 12 hr; samples were taken every other day (n = 22). The active monitor, based on the same chemical principle as the passive sampler, was designed to improve the passive method (*13,14*). This active sampler used a hollow tube denuder attached to a small personal pump (Model PAS-500, Spectrex Corp., Redwood City, CA). The denuder system consisted of a 1.4 cm (inside diameter) × 10 cm (length) etched borosilicate hollow glass tube attached to a personal pump, which maintained a constant sampling rate of 65 ml/min.

Samples were validated by examining the field and laboratory records and were removed when records justified it (e.g., broken or wet samples, unused samples, etc.). The LOD for the active method was 0.5 ppb for 12-hr monitoring during the fall study. The mean difference between the collocated active monitors was 3 ± 9 ppb (uncertainty = 7 ppb; r = 0.83). The mean difference between the collocated active and passive measurements were 0.2 ± 16 ppb (not different from zero; r = 0.48). Although the active monitors were designed to be an improved method, it was speculated that they exhibited leakage at the inlet and outlet connections in the system. Therefore, for data analysis, active measurements were vigorously screened for anomalies by removing outliers, which are defined as measurements over the 90th or under the 10th percentiles of the ratio of active to continuous measurement.

The data analysis was conducted in three major steps:

1. Descriptive statistics were performed for both spring and fall samples. Geometric means and standard deviations were calculated when skewed distributions were observed.

2. Personal exposure modeling was performed using time–activity patterns to account for differences in exposure across various microenvironments. General linear models (GLM) were used to examine random effects of day and subject on personal exposures. Personal exposure models were then developed using the microenvironmental exposure concept and multiple regression techniques. For microenvironmental modeling, average personal O_3 exposure is predicted as the sum of outdoor and indoor exposures:

$$\hat{E} = (0.8 \times C_o)F_o + (0.3 \times C_o)F_i \qquad \text{(Model 1)}$$

where $\hat{E}$ = predicted personal exposures, C_o = outdoor O_3 concentration measured at the Alpine APCD site, F_o = fraction of time spent outdoors during the daytime period, and F_i = fraction of time spent indoors (without A/C) during the daytime period.

Model 1 assumes negligible O_3 exposures while subjects were indoors with air conditioning (A/C) on because of closed windows/doors and air filters known to scavenge O_3 (*15*). The coefficients in the model are based on our earlier study results (*9*) in which the home outdoor O_3 levels were, on average, 80% of those measured at the closest outdoor monitoring sites and the mean indoor-to-outdoor ratio was 0.3.

In addition, multiple regression models were used to predict personal exposures ($\hat{E}'$) and to compare with results from Model 1:

$$\hat{E}' = \alpha_1 \times C_o \times F_o + \alpha_2 \times C_o \times F_i + \alpha_3 \times C_o \times F_a \qquad \text{(Model 2)}$$

where F_a = fraction of time spent indoors with A/C on. The split sample approach (*16*), in which samples were randomly split into two groups for model construction, was used to examine model reliability. Colinearity also was examined by calculating the condition index.

3. Factors considered to affect the prediction power of the microenvironmental models were examined and included: outdoor spatial variation, indoor O_3 concentration variation, and the measurement error resulting from analytical error and from subjects' compliance. Note that there is currently no true gold-standard measure of personal O_3 exposures. The passive monitor, in spite of being the most direct measure of personal O_3 exposure, has not been validated in natural settings in which the study subject is freely mobile. The personal passive measurements were used in this paper as a reference value for personal exposures.

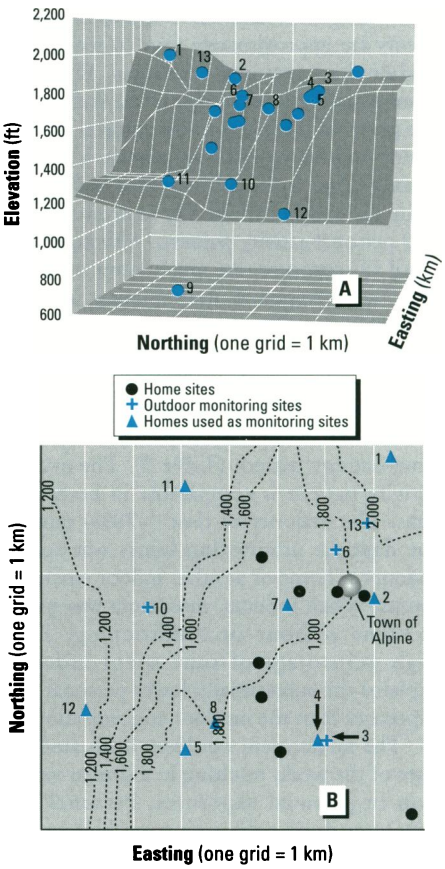

Figure 1. (A) A three-dimensional view of the study area (northing to the left for easy viewing). Filled circles represent the location of the 18 subjects' homes, the Alpine APCD site (numbered 13), and the 12 additional outdoor monitoring sites (numbered from 1 to 12). (B) The projected two-dimensional topography for the Alpine area (northing upward for conventional viewing).

Table 1. Stationary monitoring sites selected to represent the range of average weekday traffic volume and elevation in the community

	Elevation (ft above sea level)			
Traffic volume	>2,000	1,750–2,000	1,250–1,750	775–1,250
>30,000 (high)	—	Site 2	Site 6(S)	Site 9
20,000–30,000 (medium)	Alpine APCD site 13	Sites 3(S) and 4	Site 7	Sites 10(S) and 11
<20,000 (low)	Site 1	Site 5	Site 8	Site 12

Site 13 is the Alpine Air Pollution Control District continuous monitoring site; sites 3, 6, 10 were located at schools (S), while other sites were located outside subjects' homes.

Results

Descriptive statistics. During the spring monitoring period (56 days), hourly outdoor O_3 concentrations measured at the Alpine APCD site ranged between 1 and 147 ppb, averaging 49 ± 26 ppb. During the 56 12-hr daytime periods, there were 7 hr (in 5 days) when hourly O_3 concentrations exceeded the NAAQS. In the fall study, the average hourly outdoor O_3 concentration was lower than that in the spring. It ranged between 0 and 118 ppb, averaging 45 ± 20 ppb and never exceeding the NAAQS. Table 2 shows the descriptive statistics for both spring and fall 12-hr integrated samples. Outdoor measurements are approximately four to five times higher than personal exposures. Figure 2 demonstrates the variability of the daily average personal exposures across subjects for the spring and fall monitoring periods. Variance among subjects differs by day due to the variation in daily outdoor O_3 concentrations and personal activity patterns. Although personal O_3 exposures are much lower on average than continuous measurements in both seasons, the contrast is notably greater in the fall (Fig. 2B vs. 2A).

The difference between personal exposures and outdoor continuous measurements can be partly explained by the time–activity pattern (Table 3). The overall activity pattern is comparable in both seasons. The majority of time (~70%) during the daytime monitoring hours was spent indoors at home or at other indoor environments. When indoors, most time was spent at home without air conditioning. This high percentage of time spent indoors explains the substantially lower personal O_3 exposures than the outdoor concentrations.

The hours spent outdoors fluctuated by days of the week, resulting in a similar variation in personal exposures. Personal O_3 exposures during the spring are highest on Saturdays and lowest on Mondays and Tuesdays. The mean personal exposure on Saturdays is 22.6 ppb, while the mean on other weekdays and Sundays is 17.3 (two-sample t-test $p<0.001$). A similar trend was observed for outdoor O_3 measurements at the Alpine APCD site. This weekend effect has been observed in several California cities and has been attributed to weekday to weekend emission reductions in NO_x and nonmethane hydrocarbon (due to less commuter driving), which result in reduction in O_3 formation (*17*). Using the GLM for personal exposures and controlling for the subject effect, the effect of days of the week was found to be significant for both personal O_3 exposures ($p<0.001$) and activity pattern (percent time spent outdoors) ($p<0.001$) in both seasons. Evidently, personal O_3 exposures over weekends were elevated due to the greater number of hours spent outdoors and reinforced by higher outdoor O_3 levels on Saturdays and Sundays.

Modeling personal exposures. Factors that affect personal O_3 exposures were further examined with random effects GLM in which personal O_3 exposures were regressed on day of study and subject. Day-of-study and subject effects were found to be significant in both seasons ($p<0.01$). The day-of-

Table 2. Statistics for the spring and fall O_3 samples collected from subjects, the Alpine air pollution control district (APCD), the 4 colocated passive monitoring sites, and the 12 additional active monitoring sites

	Spring		Fall			
	Passive	Continuous	Passive		Active	Continuous
	Personal[a]	APCD site	Personal[a]	Stationary	Stationary	APCD site
Number	90.4	56	741	77	231	56
Mean	13.6	63.1	10.5	45.1	44.0	54.5
Median	15.5	59.7	12.7	42.9	44.9	54.5
SD	2.5	16.3	2.5	15.5	15.2	12.1

[a]Geometric statistics were justified given a lognormal distribution.

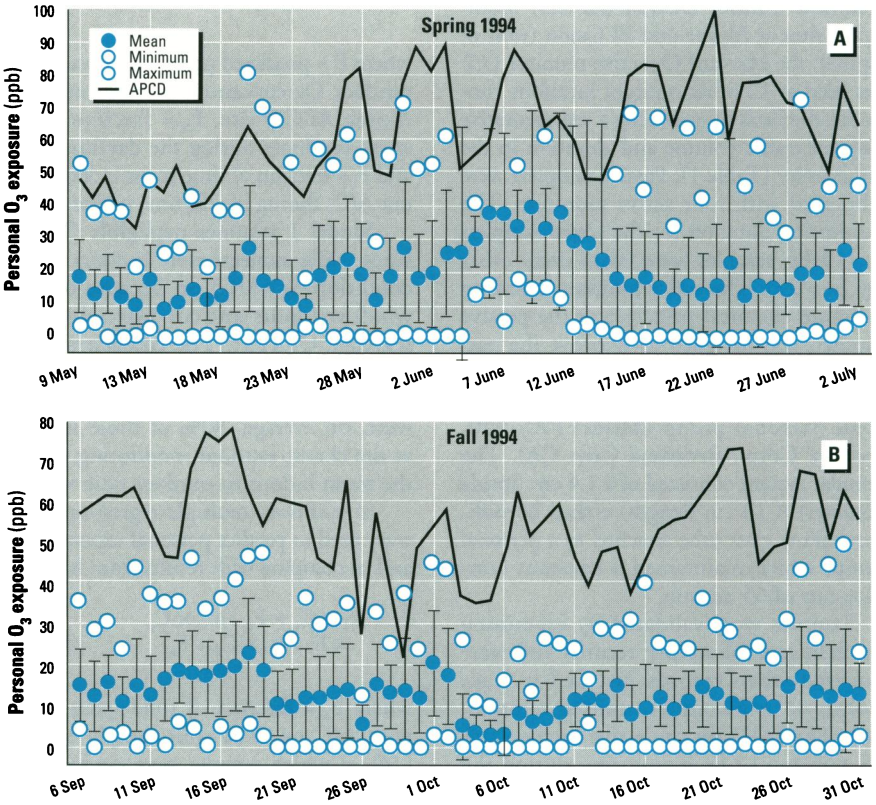

Figure 2. The daily average personal exposures across subjects. Error bars indicate SD. The outdoor Alpine air pollution control district (APCD) measurements are shown as the solid line.

Table 3. The fraction of time spent in different microenvironments during spring and fall monitoring periods[a]

Microenvironment	Air conditioning	Spring Mean ± SD	Fall Mean ± SD
Home outdoors	—	0.22 ± 0.19	0.20 ± 0.14
Outdoors in other areas	—	0.05 ± 0.13	0.03 ± 0.10
Home indoors	Off	0.59 ± 0.27	0.62 ± 0.24
	On	0.05 ± 0.15	0.07 ± 0.17
Other indoors	Off	0.05 ± 0.14	0.03 ± 0.09
	On	0.01 ± 0.06	0.01 ± 0.03
Left San Diego County	—	0.01 ± 0.10	0.00 ± 0.03
Missing or unclear data	—	0.01 ± 0.07	0.03 ± 0.14

[a]Statistics are for average time fractions across 22 subjects in the spring and 18 subjects in the fall.

study effect is a manifestation of the daily variation in outdoor O_3 concentrations and the average activities of subjects, as well as meteorological factors such as temperature, which impacts photochemical oxidation rates, subject activities, and A/C use. The subject effect reflects the variation in time–activity patterns from one subject to another. The random error accounts for unmeasured determinants of personal O_3 exposure not predicted by the subject and day variables, such as variation within activity patterns of individual subjects, compliance, and measurement errors. For spring personal exposures, the random error accounts for 59% of the variance (R^2) of individual observations, while intersubject and between-day variations comprise 18% and 23% of the variance, respectively. For fall personal exposures, the random error accounts for most (82%) of the variation in personal exposure measurements (intersubject R^2 = 9%; inter-day R^2 = 9%). These large random errors are due partly to the variation in day-to-day individual activities as well as to the low O_3 measurements.

Spring personal exposures. The results of the above GLM analysis indicate the importance of the individual activities in personal O_3 exposure modeling. This concept is illustrated with microenvironmental models that include the time–activity information as well as outdoor O_3 measurements. The predictive equation (Model 1) explains 20% (R^2 = 0.20) of the variance in the measured personal O_3 exposures. The slope of the regression line for Model 1 is almost unity (0.99 ± 0.02). The mean of the predicted values is 27.6 ppb, while the mean of the measured values is 24.7 ppb. For comparison, the regression model with the outdoor measurements (C_o) at the Alpine APCD site as the sole predictor for personal exposures resulted in an R^2 of 0.04 only (p<0.001).

The multiple linear regression equation (Model 2), which includes indoor exposures with A/C on, results in an R^2 of 0.21 (Table 4). The coefficient for outdoor exposure was 0.52, smaller than the 0.8 used in Model 1. This difference may be due to the variation in elevation and traffic counts in the community and thus the differences in outdoor O_3 concentrations between home and the Alpine APCD site. The coefficient for indoor exposures without A/C is comparable to the mean Toronto indoor/outdoor ratio (0.3). The coefficient for indoor exposures with A/C on (0.22; p<0.001) implies that indoor exposure exists even when windows are closed and the A/C is on. The R^2 value for Model 2 is low; however, when Model 2 is constructed for each subject, the resultant R^2 values range between 0.07 and 0.85. This indicates that the variation in the ability of the model to predict individual exposures is large and may be attributable to the performance of the sampler as well as the subjects' compliance to the monitoring protocol. The reliability of Model 2 is further validated using the split sample approach (*16*). The difference in R^2 values between the models that use two randomly split data sets is 0.03, and the difference in R^2 between Model 2 and the models that use either split data set is less than 0.02.

Fall personal exposures. The same modeling effort was carried out for fall personal exposures. First, outdoor measurements, C_o at the Alpine APCD site, are used to predict personal exposures ($\hat{E}$), resulting in an R^2 of 0.07 ($\hat{E}$ = 0.23 C_o; p<0.001). A similar R^2 of 0.06 (p<0.001) is found when Model 1 is used to predict personal exposures, with model predictions generally overestimating personal exposures (estimated = 20.5 ± 7.9 ppb; measured = 12.7 ± 10.2 ppb; n = 663). The slope of the regression line for the predicted versus measured values is 1.06 ± 0.03. This higher random error in the fall model as opposed to the spring model may be attributable to the lower personal O_3 exposures, which may result in a higher measurement error.

The multiple linear regression model (Model 2) results in an R^2 of 0.09 (Table 4). The split sample approach also was used to examine the model reliability. The difference in R^2 values between the split data sets is 0.01, demonstrating the reliability of the model. For Model 2, the regression coefficients from the fall data are smaller than those used for Model 1. In particular, the coefficient for indoor exposure with A/C off (E_i) is smaller than that with A/C on (E_a). The adequacy of the regression model regarding potential colinearity problems was further examined by calculating the condition indices. Results show small condition index values for all independent variables (≤8), indicating that colinearity is not a problem in the models and that coefficients are stable; however, we suspect that the regression coefficients for indoor exposures with A/C on or off are inaccurate. It was observed during the study that despite instructions, young subjects might not have accurately recorded the use of A/C at school. The following sections investigate further possible modeling errors for the fall study results.

Time–Activity Patterns Versus Exposures

The results of our study show that peak O_3 concentrations occur at times when subjects are likely to be outdoors, as shown in Figure 3. Therefore, peak exposures should occur between 11 A.M. and 1 P.M., when subjects were likely to be outdoors. However, even at the peak of the outdoor activity profile, less than 35% of the time was spent outdoors. Therefore, subjects were generally not exposed to the high outdoor O_3 concentrations as would have been measured by the outdoor monitors.

In addition to the hour of the day, whether subjects spent their time outdoors also depended on the temperature. As shown in Figure 4, outdoor activities increase with temperature between 50 and 70°F. When the temperature is higher than

Table 4. Coefficients and R^2 values for Model 2 using the entire data set for predicting personal O_3 exposures in spring and fall

Season	Variable	Coefficient	Number	Mean	Model		R^2
					F-value	*p*-value	
Spring	E_o	0.52 ± 0.02*	523	24.69	45.36	<0.0001	0.21
	E_i	0.33 ± 0.01*					
	E_a	0.22 ± 0.04*					
Fall	E_o	0.39 ± 0.03*	652	12.79	21.38	<0.0001	0.09
	E_i	0.18 ± 0.01*					
	E_a	0.25 ± 0.04*					

Abbreviations: E_o, outdoor exposure; E_i, indoor exposure without air conditioner; E_a, indoor exposure with air conditioner on.
*p <0.001.

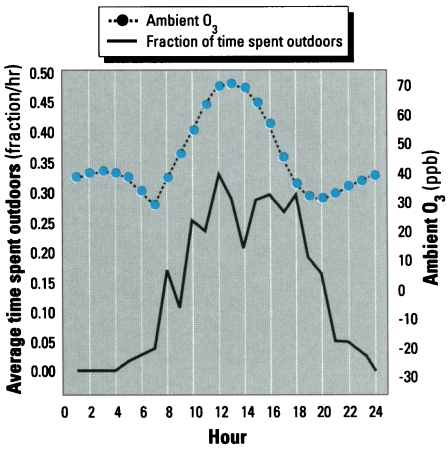

Figure 3. The average outdoor activity profile (fraction of time spent outdoors during each hour) and the outdoor O_3 concentrations in the fall. (Note that the tails of the activity profile span over the nominal 12-hr daytime monitoring period to include activities from those who awoke early or late.)

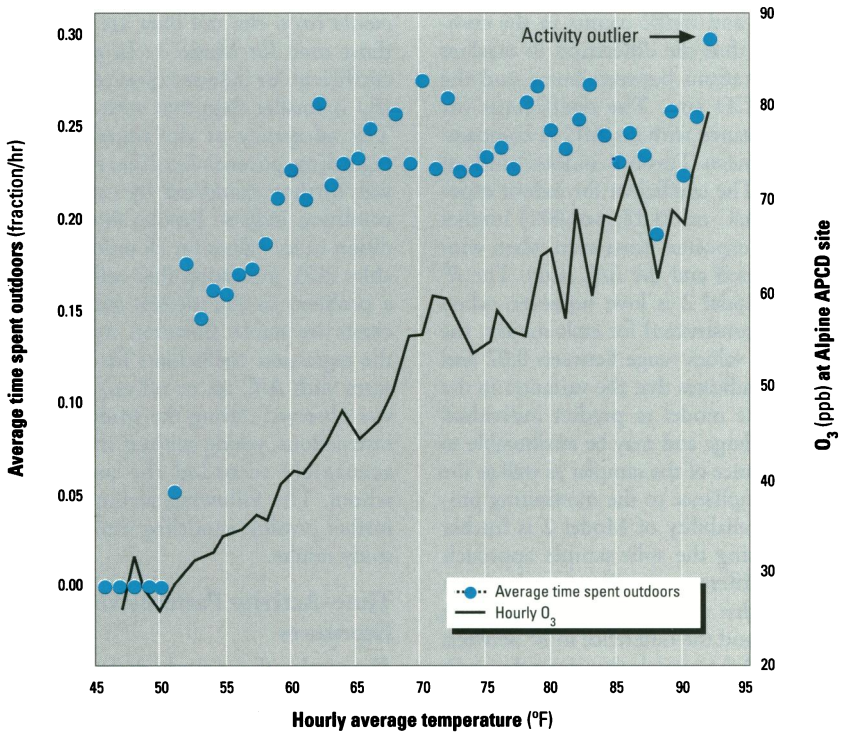

Figure 4. Average fraction of time in the hour spent outdoors for all subjects and outdoor O_3 concentrations measured at the Alpine air pollution control district (APCD) site as a function of temperature.

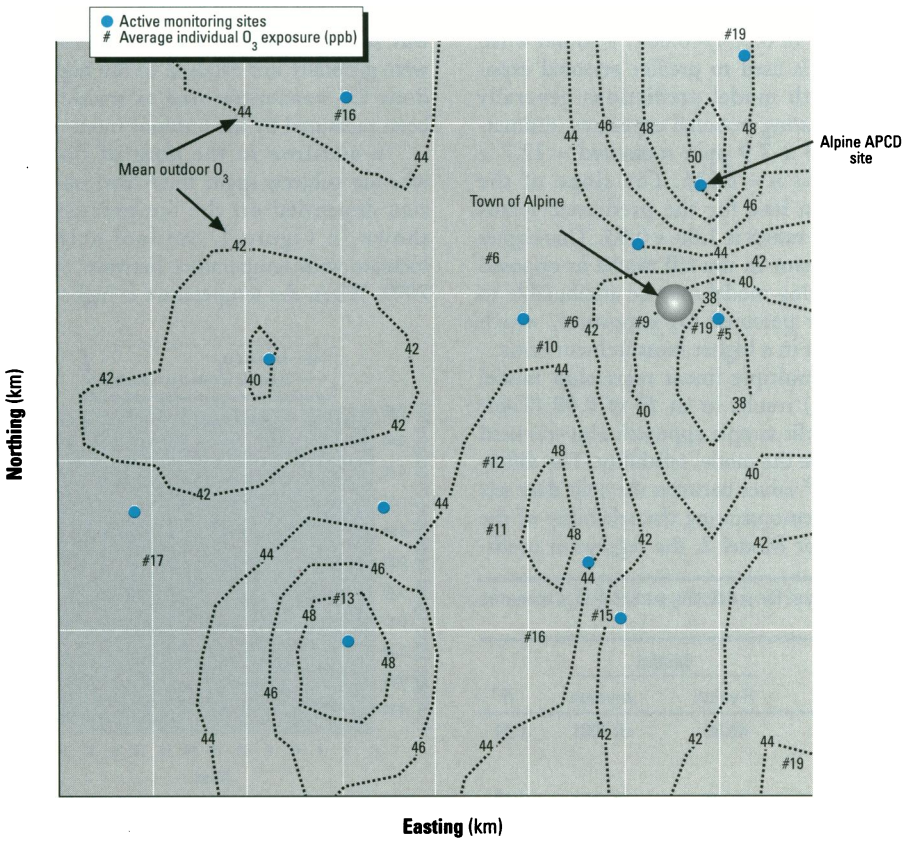

Figure 5. Contour plot of the average outdoor O_3 concentrations measured at the 13 outdoor active sites over the fall study period. # Indicates the average exposure for each individual during the fall, shown at the subject's home location. APCD, air pollution control district.

70°F, outdoor activities reach a plateau and decrease slightly at very high temperatures except for one high outdoor-activity outlier, which occurred primarily (95% of the observations) on Saturdays. Subjects tend to remain indoors to escape high temperatures; thus they unintentionally avoid high O_3 exposures. We expected that the percentage of A/C usage would be high while subjects were indoors and outdoor temperatures were high, especially during school hours. Although the reported A/C usage (percent of time A/C on while subjects are indoors) and the corresponding hourly outdoor temperature are well correlated (R^2 = 0.88), no more than 35% of the subjects reported using A/C even when the temperature exceeded 90°F. While this may be true at home when electricity costs are a concern, it should not be the case at the four schools in the area where the A/C is operated either manually by teachers or automatically. Reporting errors could have contributed to the low percentage of A/C use, which in turn results in an overestimation of personal O_3 exposure in the above models. To adjust for this potential bias, we developed a model by assuming that there is a linear relationship between A/C use and outdoor temperature and that most A/Cs are on at temperatures greater than 80°F. However, with this A/C model, the predictive power (R^2) of Model 1 was not improved, although the mean of the predicted values is closer to that measured. We also further examined the first term in Model 1 ($0.8 \times C_o \times F_o$), i.e., the spatial variation in O_3 exposure in relation to the stationary site levels.

Spatial Variation

Continuous measurements. Because of the high altitude, O_3 concentrations at the Alpine APCD site (622 m, mean O_3 = 54 ppb) are always higher than those at the nearby El Cajon APCD site (200 m, mean O_3 = 41 ppb). In addition, O_3 levels at these two locations did not follow the same trend. The correlation between these two continuous measurements depends on the averaging time period. The R^2 for hourly O_3 concentrations at these two sites is 0.38. The R^2 decreases when longer averaging durations for O_3 concentrations are used, especially when averaging duration extends into early morning (before 7 A.M.) or late evening (after 7 P.M.). It is possible that the radiation inversion layer may at times be lower than the Alpine APCD site, especially after sunset and before sunrise. In this case, O_3 aloft did not mix with the air underneath, resulting in higher O_3 concentrations at the higher altitude Alpine APCD site than at the El Cajon APCD site. This observation may explain in part

the low R^2 for exposure models based on stationary measurements.

Active measurements. The spatial pattern of outdoor O_3 concentrations in the Alpine area is further examined using the active O_3 measurements at the additional monitoring sites (Fig. 1). The contour plot for the average outdoor O_3 concentrations in fall (Fig. 5) shows that sites near the town of Alpine have the lowest O_3 concentration while sites at the highest elevations have the highest O_3 concentration. Table 5 summarizes O_3 concentrations at different elevations and traffic conditions. The mean outdoor O_3 concentrations at elevations less than 600 m are comparable. The mean concentration for sites located at elevations greater than 600 m is on average 10 ppb higher than others. Ozone concentrations at locations in low to medium traffic areas are on average 5 to 6 ppb higher than those located in heavy traffic areas. The GLM results indicate that after controlling for the effect of day of study, both traffic ($p<0.01$) and elevation ($p<0.001$) trends are significant. To predict O_3 concentrations at the active sites, continuous measurements at the Alpine APCD site are first used as the only predictor in a regression model ($R^2 = 0.49$). However, the multiple regression model, which includes traffic conditions (1, light; 2, medium; 3, heavy), distance between the active and Alpine APCD sites, and elevation, only improves the predictions slightly ($R^2 = 0.53$).

Personal measurements. The cross-sectional correlation was calculated to further compare personal exposures with the Alpine APCD site measurements. The R^2 varies substantially by subject, ranging between 0 and 0.25. The low R^2 may be attributed in part to the spatial variability in outdoor O_3 concentrations. Figure 6 shows the relationship between individual R^2 values and the distance between the subject's home and the Alpine APCD site. A decreasing correlation with distance for possibly two groups of subjects is observed. The first group, above the fitted curve, exhibits a higher correlation with the Alpine measurements even at distance as far as 12 km. The second group shows a rapid decrease in R^2 with distance. Most subjects in the first group (five out of six) live in areas with low to medium traffic, which are comparable to the traffic conditions at the Alpine APCD site. This contrasts with the second group, with subjects living in areas with medium to heavy traffic.

To examine the effect of this spatial variability, the microenvironmental model is modified by adding predictive factors, including traffic conditions, three-dimensional distance from the home (or school for students during weekdays) to the Alpine APCD site, and the difference in elevation between the home (or school) and the Alpine APCD site (Table 6). Because subjects tended to be outdoors during O_3 peak hours (Fig. 3), the daily 1-hr maximum O_3 concentration is also used as a predictor. The ability to predict personal exposures for the models using the APCD site 12-hr mean O_3 (Model 3, Table 6) is not notably different from that using the APCD site 1-hr maximum O_3 measurements (Model 4, Table 6).

When distance, difference in elevation, and traffic conditions are added (Model 5, 6, Table 6), the adjusted R^2 increased twofold. To advance the modeling effort, school site measurements as well as the spatial interpolation model predictions, including kriging and inverse distance predictions, were used to predict outdoor O_3 concentrations. The predicted values were then used in Models 5 and 6 (Table 6) to replace C_o. However, these models did not improve the R^2 values.

Table 5. Summary statistics of O_3 concentrations at different elevations (grouped for equal sample size) and traffic density

		Ozone concentration (ppb)				
Parameter	Level (m)	No.	Mean	SD	Minimum	Maximum
Elevation	<400	57	42.0	14.8	9.7	71.6
	500–550	58	42.9	14.0	12.4	64.1
	551–600	69	43.7	16.0	9.0	97.0
	601–700	76	53.0	13.3	17.5	77.6
Traffic	Low	75	46.4	15.8	14.8	97.0
	Medium	101	45.0	14.6	9.7	73.3
	High	57	40.5	14.1	9.0	68.4

SD, standard deviation.

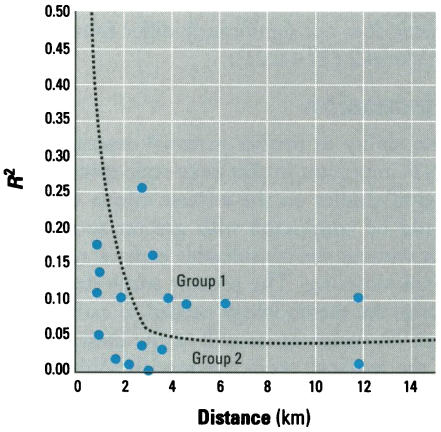

Figure 6. R^2 for personal exposures and the Alpine air pollution control district (APCD) site measurements for individual subjects as a function of the three-dimensional distance between the subjects' home and the Alpine APCD site. (Note that subjects did not always stay home and that the distances are only an approximation.) Curve fit: $R^2 = 0.04 + e^{-0.95x}$.

Table 6. Microenvironmental models for personal exposures during the fall study period

Model	Variable	Major predictor (C_o)	Coefficient	Adjusted R^2
3	Intercept	Mean O_3	0.52 ± 1.78	0.10
	E_o		0.36 ± 0.05**	
	E_i		0.17 ± 0.03**	
	E_a		0.23 ± 0.05**	
4	Intercept	Maximum O_3	0.52 ± 1.58	0.11
	E_o		0.25 ± 0.03**	
	E_i		0.13 ± 0.02**	
	E_a		0.16 ± 0.03**	
5	Intercept	Mean O_3	3.59 ± 2.85	0.17
	E_o		0.32 ± 0.04**	
	E_i		0.19 ± 0.03**	
	E_a		0.21 ± 0.05**	
	Traffic		-2.37 ± 0.79*	
	Distance		1.43 ± 0.42**	
	dZ		0.02 ± 0.01**	
6	Intercept	Maximum O_3	3.45 ± 2.72	0.19
	E_o		0.22 ± 0.03**	
	E_i		0.13 ± 0.02**	
	E_a		0.14 ± 0.03**	
	Traffic		-2.29 ± 0.78*	
	Distance		1.45 ± 0.42**	
	dZ		0.02 ± 0.01**	

Abbreviations: E_o, outdoor exposure, $C_o \times F_o$; E_i, indoor exposure without A/C, $C_o \times F_i$; E_a, indoor exposure with A/C on, $C_o \times F_a$; Traffic, traffic condition near subject's home (high, medium, and low); Distance, distance between home and the Alpine APCD sites (km); dZ, elevation difference between home and the Alpine APCD sites (m). C_o is the 12-hr mean (Model 3, 5) or hourly maximum (Model 4, 6) O_3 concentration at the Alpine APCD site.
*p-value <0.01.
**p-value <0.001.

Colinearity was examined for all models. The highest correlation between the independent variables is 0.64 between distance and elevation difference. The tolerance values for all independent variables are greater than 0.1 and the condition index values are smaller than 20. Therefore, colinearity is not evident for any models. For the spring model, when additional variables for distance, elevation, and traffic conditions were added to predict 12-hr personal exposures, the R^2 (adjusted R^2 = 0.22; significant predictors include outdoor and indoor exposures, traffic, and distance) does not significantly differ from that of Model 2 (R^2 = 0.21).

Discussion

The ability to predict personal exposure to O_3 is important in that large-scale epidemiological studies on the adverse effects of O_3 could be conducted with greater accuracy but without the considerable expense of personal sampling. The present study demonstrates the methodology needed to carry out such an endeavor, as well as the limitations of the resultant predictive models. Although the models reported here are unlikely to fulfill the need for accurate exposure assessment in an epidemiological setting, they do provide valuable insight into the determinants of O_3 exposure and the relevance of outdoor stationary site measurements to exposure.

For instance, personal exposures to O_3 were found to differ by the days of the week. More time is spent outdoors on weekends, when outdoor O_3 concentrations are higher, than on weekdays. During the daytime period, more time is spent outdoors during the period when outdoor O_3 peaked. Personal exposures are therefore enhanced by such activity patterns. Nevertheless, subjects do not spend a significant percentage of time outdoors (<35% at the peak of the activity profile). Since most of the time is spent indoors, cumulative indoor O_3 exposures are important. Indoor O_3 concentrations, however, vary with the ventilation conditions and home characteristics. Although deposition of O_3 on clothes may result in a reduced personal measurements on the passive sampler (*12*), the analysis on time–activity pattern suggests that the low personal exposure is not an artifact but a manifestation of the low fraction of time spent outdoors.

The R^2 between the Alpine and El Cajon APCD sites ranged between 0.37 and 0.53, while the R^2 for Models 1 through 6 ranged between 0.08 and 0.22. The lower R^2 values for these microenvironmental models can be explained by the fact that the outdoor monitors are fixed and thus easier to predict while subjects move around different microenvironments with various O_3 concentrations. In addition, personal exposure measurements were not made at fixed times and durations. The analyzed personal measurements include sampling durations between 9.6 and 14.4 hr (within a 20% range of 12 hr), starting between 6 and 10 A.M. Furthermore, the low R^2 may also result from the measurement error due to different effective collection rates of the passive sampler in various environments (*12*). Correlations between personal exposures and the outdoor measurements varied among subjects due to various activity patterns and geographical and demographic characteristics near the home, school, or workplace. Intrasubject variance and monitoring error probably account for most of the variability in personal exposures. Less than 40% of the variance in personal O_3 exposure was attributed to intersubject and day-of-week variabilities.

Based on outdoor concentrations obtained from the Alpine APCD site and time–activity information collected from the subjects, simple personal exposure models predict 20% and 6% of the variability in the measured personal exposures in spring and fall, respectively. Although such predictive powers are low, the models are reliable when assessed by the split sample method. Inaccurate time–activity information on the use of air conditioning might have contributed to the low R^2. Efforts will have to be made in the field to correct this A/C reporting error, such as taking daily air exchange rate measurements or collecting information on A/C use from workplaces and the school. In addition, the spatial variation of O_3 also resulted in variation in personal O_3 exposures in the study area. By adding factors that are associated with the spatial variation to the simple personal exposure models, the R^2 was markedly improved from 0.06 to 0.19 for the fall data. Similar modeling efforts, however, only resulted in a minimal improvement of the predictions for the spring data. It is possible that measurement error from the personal monitor and the time–activity records accounts for most of the variance in personal measurements.

Conclusions

Key findings of this study include the following:

- Personal O_3 exposure differs dramatically (by fourfold on average) from outdoor stationary O_3 measurements (Fig. 2) and is not predicted well by these outdoor measurements (R^2 = 0.07 or less).
- There is considerable intersubject variability in personal O_3, which is partially explained by differences in percent of time spent outdoors.
- Models perform differently by season; microenvironmental Model 1 and multiple regression Model 2 for spring cohorts have two to three times the R^2 of the fall cohorts.
- The fall, but not the spring, model was markedly improved by adjusting for distance from the outdoor stationary site.

Recent studies (*8,9,18,19*) that examine associations between personal exposures and outdoor measurements found similar values for R^2. Thus, microenvironmental models including outdoor O_3 concentrations and simple personal activity information are improvements in estimating personal exposures over models including only outdoor stationary site measurements. Predicting personal exposures was further improved by the inclusion of microenvironmental variables such as spatial variation and workplace (e.g., school) exposures in the present and past O_3 modeling studies (*9*). However, it remains to be shown to what degree such predictive models enhance the ability to detect the adverse respiratory health effects of O_3 in an epidemiological study that would otherwise rely on outdoor stationary site O_3 measurements.

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Environmental Health Perspectives
Vol. 18, pp. 141-146, 1976

Studies in Adaption to Ambient Oxidant Air Pollution: Effects of Ozone Exposure in Los Angeles Residents vs. New Arrivals

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To test the hypothesis that adaptation protecting against acute effects of ambient ozone (O_3) exposures develops in Los Angeles residents, human volunteers were exposed to 0.4 ppm O_3 under conditions simulating ambient pollution exposures. Blood biochemical, pulmonary physiological, and clinical responses were assessed. Los Angeles residents ($N = 6$) showed only minimal clinical or physiological response to O_3, while new arrivals ($N = 9$) showed significant losses in pulmonary function and a tendency toward increased symptoms. Most biochemical responses did not differ significantly between residents and new arrivals. These results agree with others in suggesting that exposures to elevated ambient concentrations of O_3 produce adaptation in at least some residents of photochemical pollution areas. The underlying mechanisms and long-term consequences of such adaptation are unknown.

Introduction

Development of tolerance to ozone (O_3) and other irritant gases in experimental animals was first described by Stokinger and co-workers approximately 20 years ago (*1*) and has been studied extensively since. The subject has been reviewed by Fairchild (*2*) and Morrow (*3*). Salient features of animal tolerance include the following. Pretreatment with a relatively low O_3 dose will prevent death or severe lung injury which would otherwise occur with a higher dose. This tolerance gradually disappears after cessation of O_3 exposure. Cross tolerance exists among O_3 and other irritant gases, including some which, like O_3, are powerful oxidizing agents and others which are not. Tolerance does not prevent the development of chronic lung lesions following repeated exposures. Tolerance results in decreased edema formation in response to O_3 challenge, but no diminution of cytotoxic effects of O_3 is observable (*4*). The biological mechanisms responsible for tolerance are largely unknown.

The observation that animals can respond to a toxic inhalation challenge in a manner which prevents some of the short-term adverse effects of further exposures suggests the possibility that an analogous response might occur in humans exposed to community air pollution. We use the term "adaptation" to describe this hypothetical response in humans, since the doses of toxicants being considered are much less than in animal "tolerance" studies, and since responses are less severe and perhaps depend on different biological phenomena. Metropolitan Los Angeles experi-

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ences uncommonly high ambient levels of O_3 and other oxidants during photochemical smog episodes; thus residents of this area constitute an attractive group in which to investigate the possibility of adaptation. That Los Angeles residents suffer less deleterious effects of ambient exposures than visitors to the area has been previously suggested (*5*), but the hypothesis has never been tested extensively.

Previous work in our laboratory (*6,7*) showed that some healthy Los Angeles residents develop respiratory symptoms and function changes when exposed to O_3 concentrations of 0.37-0.50 ppm—less than maximum ambient concentrations in the area. Similar studies in Canadians not frequently exposed to ambient oxidants (*8,9*) appeared to show a greater mean effect of a given dose, suggesting that responses in Los Angeles residents might have been reduced by adaptation. Methodological differences between studies might have explained the apparently different response, however. To test this possibility, a cooperative investigation was undertaken to compare experimental methods and responses of a small sample of subjects to 0.4 ppm O_3 (*10*). The results reproduced to a great extent the previous finding of less reactivity in Los Angeles residents as compared to Canadians and failed to reveal any methodological factors which could account for this difference. The hypothesis of adaptation was thus supported. To test the hypothesis more rigorously, the present study was undertaken in order to compare the effects of 0.4 ppm O_3 in somewhat larger and more carefully matched groups of Los Angeles residents and nonresidents.

Methods

The null hypothesis tested was as follows. Healthy Los Angeles residents (three years or more in area) and new arrivals (five days or less in area) will not differ in mean clinical, physiological or biochemical response to 0.4 ppm O_3 exposure under conditions simulating ambient pollution episodes. Rejection of the null hypothesis with new arrivals showing significantly greater mean response would be the necessary result if the hypothesis of O_3 adaptation in residents were to be supported.

The exposure facility and basic experimental design have been described in detail previously (*11*). Volunteer subjects were studied on two successive days. The first day's exposure was to purified air only; the second day's exposure was to 0.40 ppm O_3 in purified air. Exposures lasted 2 hr 15 min. During the first 2 hr, each subject exercised at a workload sufficient to increase minute volume to approximately twice the resting level (150-200 kg-m/min) for 15 min in every half hour. During the last 15 min pulmonary function tests were performed; these included forced vital capacity (FVC), one-second forced expiratory volume (FEV_1), maximum midexpiratory flow rate (MMF), total respiratory resistance by forced oscillation (R_t), and indices of the single-breath nitrogen test: closing volume as a percent of vital capacity (CV/VC), and slope of the alveolar plateau (ΔN_2). Each subject's test results were expressed as control values (those obtained after purified-air exposure) and as O_3 responses (differences between post-O_3 exposure and control values). Subjects' symptoms during and following exposure were recorded and scored semiquantitatively according to severity and duration using a standard interview questionnaire administered by the project medical officer. The symptom response to O_3 was expressed as the difference in symptom score between O_3 exposure and control days. Venous blood samples were drawn immediately following exposure, and erythrocyte (RBC) and serum analyses were performed to detect changes expected to result from an oxidant challenge, as described previously (*12*).

Paired statistical tests with each subject serving as his own control were applied to detect differences between control and O_3 conditions for the resident group and for the new-arrival group. Unpaired tests were applied to compare between groups. For physiological measures, only O_3 responses were compared between groups, as control values were expected to depend mostly on body size and not on adaptation. For biochemical measures, control values could have differed between groups as a consequence of adaptation, therefore both control values and O_3 responses were compared statistically. In addition to the commonly employed *t* tests, analogous nonparametric tests—the Wilcoxon signed-rank test for paired analyses and the Mann-Whitney U test for between-group analyses—were applied to the pulmonary function data. The nonparametric tests were expected to be possibly more powerful in analyzing these data since the data were expected to be skewed, whereas *t* tests require a normal distribution for greatest reliability. Skewness is inherent in data of this nature since there is considerable variability between individuals in reactivity to exposure, and since

function measures remain similar to control values in relatively unreactive subjects but deviate from control values in only one direction in more reactive subjects. Symptom data, which were not rigorously quantitative and not necessarily expected to show a normal distribution even under control conditions, were analyzed only with the nonparametric tests.

Subjects were recruited within the incoming 1975 class of the USC School of Physical Therapy. Fifteen of a possible 44 individuals volunteered to be studied; six of these were residents of metropolitan Los Angeles and nine were nonresidents. Studies were conducted during September, i.e., late in the summer smog season when residents should have had ample time to develop adaptation. Nonresidents were studied within five days of their arrival in Los Angeles; they were instructed to minimize intercurrent ambient oxidant exposures by remaining in coastal areas of metropolitan Los Angeles and/or remaining indoors and at rest during peak oxidant hours.

Individual subject characteristics are given in Table 1. Since the nonresidents included two males, while the residents were all female, the possible effect of sex differences on the overall results was examined. The males' data were compared individually with the female nonresidents' for the three measures which showed significant ($p < 0.05$) group differences. Both males' values fell within the females' range, except that one male had the largest control and post-exposure FEV_1. When statistical analyses were repeated excluding the males' data, mean group responses were actually larger than when the males were included; however, due to the reduction in sample size the level of significance of the group differences decreased—$0.05 < p < 0.10$ with males excluded. Overall, no evidence was found that sex differences affected the results; this was also the case in the previous study (*10*).

Results

Individual physiological and clinical responses are given qualitatively in Table 1, and group mean physiological and symptom measures are summarized in Table 2. The residents as a group showed no significant O_3 responses except for slight decrease in ΔN_2. Increases in ΔN_2 are normally expected in chronic pulmonary dysfunction and in acute responses to O_3 exposure (*6*). Decreased values represent increased uniformity of ventilation distribution and thus could be considered an improvement in function. On the other hand, more uniform distribution could be the result of adverse physiological changes, such as complete "closure" of a few small airways previously only partially obstructed. Nonresidents

Table 1. Individual subject characteristics.

I.D. No.	Sex	Age, yr.	Ht., in.	Wt., lb.	Smoking	Years in Los Angeles area	O_3 response [a]
Los Angeles residents							
52	F	22	69	158	current	18	–
59	F	25	68	118	–	3	P
60	F	25	68	118	former	18	S
65	F	21	67	138	–	10	P
66	F	25	63	94	–	3	–
69	F	22	65	125	–	14	–
Nonresidents (new arrivals)							
47	F	22	68	140	–	–	P,S
49	M	22	71	160	–	–	P,S
50	F	21	66	115	–	b	–
51	F	21	62	125	–	–	P,S
53	F	22	73	155	–	–	–
55	F	22	68	125	–	–	S
56	F	23	62	120	–	–	P,S
57	F	21	64	121	–	–	P
58	M	24	72	170	current	–	P

[a] P = physiological response—significant ($p<0.05$) loss in FVC and/or FEV_1 with 0_3 exposure relative to control, determined by t test, three measurements under each condition. S = symptom response—increase in symptom score of ≥ 4 units (arbitrary definition of "clinically significant" response).

[b] Spent previous summer in area.

Table 2. Comparative pulmonary function and symptom measures: control values with O_3 exposure[a]

	Residents	New arrivals	Intergroup comparison	
			t	U
Control FVC, l	4.01 ± 0.40	4.57 ± 0.89		
FVC change, l	−0.093 ± 0.155 [b]	−0.164 ± 0.202 [c]	0.72 [b]	20 [b]
Control FEV_1, l	3.49 ± 0.22	3.84 ± 0.49		
FEV_1 change, l	−0.018 ± 0.098 [b]	−0.171 ± 0.174 [c]	1.93 [b]	9($p<0.05$)
Control MMF, l./sec	4.06 ± 0.70	4.23 ± 0.86		
MMF change, l./sec	+0.175 ± 0.336 [b]	−0.252 ± 0.320 [c]	2.48($p<0.05$)	9.5($p<0.05$)
Control CV/VC %	7.6 ± 5.5	6.8 ± 5.8		
CV/VC change, %	+0.4 ± 2.8 [b]	+0.5 ± 3.2 [b]	0.12 [b]	24 [b]
Control ΔN_2, % N_2/l	0.95 ± 0.15	0.93 ± 0.23		
ΔN_2 change, % N_2/l	−0.117 ± 0.094 [d]	−0.050 ± 0.206 [b]	0.73 [b]	21.5 [b]
Control R_n, cm H_2O/(l./sec)	4.02 ± 0.99	3.25 ± 0.90		
R_n, change, cm H_2O/(l./sec)	+0.13 ± 0.98 [b]	+0.20 ± 0.45 [b]	0.18 [b]	17 [b]
Control symptom score	4.9 ± 5.1	3.6 ± 3.5		
Symptom score change	+0.2 ± 5.5 [b]	+2.7 ± 4.8 [b]	—	19 [b]

[a] Means ± S.D.
[b] Not significant.
[c] Significant decrement after exposure, $p<0.05$ by paired *t* test and by Wilcoxon signed-rank test.
[d] Change not significant by signed-rank test; apparent "improvement" after exposure according to paired *t* test ($p<0.05$).

showed a smaller, nonsignificant decrease in ΔN_2, but showed significant O_3 responses in FVC, FEV_1, and MMF. The MMF response was significantly more severe than in the residents according to the intergroup comparison, but the FVC responses did not differ significantly between the groups. The FEV_1 loss was significantly more severe in nonresidents than in residents according to the U test ($p = 0.03$), but not according to the *t* test ($p = 0.06$). Since the distributions of FEV_1 responses appear skewed (Fig. 1), the results of the U test may be more reliable. Neither group showed significant responses of CV/VC, R_n, or symptom score, but the nonresidents showed a trend toward increased symptom score with O_3 exposure.

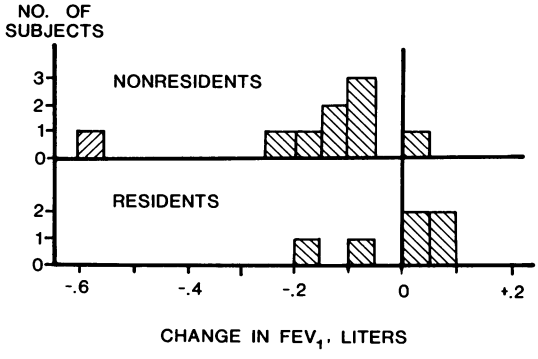

FIGURE 1. Histograms of O_3 responses in FEV_1 (change between post-exposure and control measurements) for nonresidents and residents. Number of subjects showing a given response (within a 0.05-l. interval) vs. magnitude of response.

Group mean biochemical measurements and significant changes related to exposure are summarized in Table 3. None of the analyses showed significant differences in control values between residents and new arrivals, although residents showed trends toward less fragility of RBCs as determined by hydrogen peroxide challenge, and higher serum concentrations of Vitamin E. Both groups showed O_3 responses generally similar to those seen previously (*12*): increased RBC fragility, reduced RBC acetylcholinesterase activity, and tendencies toward increased activity of pentose pathway enzymes (which would tend to protect against excessive oxidation of cellular components). Lactate dehydrogenase (LDH) activity was the only biochemical measure to show a significant difference between groups in response to O_3. New arrivals showed the expected increase in LDH activity, while residents showed a decrease, in contrast to previous findings (*12*). The biological significance of this observation, if indeed it represents other than a chance occurrence, is unclear.

Discussion

These results support the hypothesis of adaptation to O_3 in Los Angeles residents. Statistical differences found between residents and new arrivals are relatively small, as should be expected given the unavoidably small sample sizes and the

Table 3. Comparative biochemical measures: control values and change with O_3 exposure.[a]

		Residents	Intergroup comparison[b] New arrivals	t
RBC fragility,	Control	23.0 ± 15.2	31.4 ± 8.0	1.39[c]
% hemolysis in H_2O_2	Change	+6.2 ± 5.5[d]	+3.1 ± 3.4[d]	1.35[c]
RBC acetylcholinesterase,	Control	17.5 ± 1.8	18.8 ± 1.9	1.31[c]
mmole/ml/min	Change	−0.6 ± 0.6[e]	−0.8 ± 0.5[f]	0.83[c]
RBC glutathione,	Control	33.3 ± 6.2	35.3 ± 5.0	0.67[c]
mg %	Change	−1.6 ± 1.9[c]	−2.0 ± 3.0[c]	0.28[c]
RBC 2,3-diphospho-	Control	14.9 ± 1.6	14.7 ± 4.1	0.12[c]
glycerate, μmole/g Hb	Change	−1.7 ± 0.7[f]	+1.0 ± 3.3[c]	0.50[c]
RBC glucose-6-phosphate	Control	5.22 ± 1.14	5.05 ± 0.86	0.33[c]
dehydrogenase, U/g Hb/min	Change	+0.23 ± 0.43[c]	+0.21 ± 0.32[c]	0.09[c]
RBC lactate dehydrogenase,	Control	107 ± 16	112 ± 15	0.59[c]
U/g Hb/min	Change	−6.6 ± 12.4[c]	+8.9 ±9.5[f]	2.74[g]
RBC glutathione peroxidase,	Control	8.6 ± 1.8	8.8 ± 1.7	0.23[c]
U/ml/min	Change	+0.8 ± 1.1[c]	+0.3 ±0.8[c]	1.11[c]
Serum Vitamin E,	Control	2.77 ± 0.79	2.64 ± 0.38	0.44[c]
mg %	Change	+0.09 ± 0.15[c]	+0.03 ± 0.14[c]	0.66[c]
Serum glutathione	Control	23.7 ± 4.2	22.6 ± 3.0	0.60[c]
reductase, mU/ml/min	Change	+1.5 ± 1.7[c]	+2.8 ±3.0[f]	0.98[c]

[a] Means ± S.D.
[b] Intergroup comparisons by U test gave same results as t test in every case, with respect to significance at 0.05 level.
[c] Not significant.
[d] Significant ($P<0.05$) change after exposure by t test; not significant ($0.05<P<0.10$) by signed-rank test.
[e] Significant ($P<0.05$) change after exposure by signed-rank test; not significant ($0.05<p<0.10$) by t test.
[f] Significant ($p<0.05$) change after exposure by t test and by signed-rank test.
[g] Significant difference between groups ($p<0.05$).

typically large individual variability in O_3 responses. Controlled-exposure studies cannot be done on a large enough scale to conclusively establish differenes in response between populations, but the essetial agreement of present and previous results in small-scale studies considerably strengthens the case for the existence of such differences. Various factors unrelated to inherent adaptive biological reponses could explain these results—selective migration or diet, for example (*10*). No such factor has yet been identified, leaving adaptation as the most plausible explanation for the experimental observations. No biochemical index of the adapted state has yet been found in animals or in man, nor are the physiological and biochemical mechanisms of O_3 toxicity well understood. Further investigations in these areas will be necessary before the biological mechanisms of the adaptive response (if it exists) can be elucidated. Of particular interest is the possibility that adaptive mechanisms may be inoperative in certain individuals, who might then be at increased risk of developing chronic respiratory disease.

The phenomenon of adaptation may ultimately, but should not presently, be taken into account in setting ambient or occupational air-quality standards. By analogy with animal studies, it appears that human adaptation to acute O_3 effects might not protect against the possible development of chronic lung damage after many exposures. Unless this possibility and the possibility of failure of adaptation are conclusively ruled out, air quality standards should continue to be set to protect the susceptible, least well-adapted individuals in the exposed population.

From the Specialized Center of Research in Environmental Lung Disease (SCOR), National Heart and Lung Institute, Grant No. HL-15098-05.

This paper was presented in part at the Conference on Recent Developments in Toxicity of Environmental Oxidants, National Institute of Environmental Health Sciences, Bethesda, Maryland, March 4-5, 1976.

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