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Merced / Mariposa County Asthma Coalition
*Controlling asthma through awareness and education*



April 21, 2009

Kim Espinosa
City of Merced - Planning Department
678 W. 18th
Merced, CA 95340

**Re: The Merced/Mariposa County Asthma Coalition Opposes the Proposed Wal-Mart Distribution Center**

Dear Ms. Espinosa,

The Merced/Mariposa County Asthma Coalition (MMCAC) is a community-based health organization that is composed of a diverse membership of over 150 volunteer members that seek to fulfill our mission of *controlling asthma through awareness and education.* Since 1997, the coalition has implemented both clinical and environmental interventions which help to reduce the prevalence of asthma in our community by working with schools, health care professionals, policymakers and residents. MMCAC members have a proud history of advocating for the strongest, most health-protective policies possible on the local, regional and statewide levels.

Since plans for the Wal-Mart distribution center were first announced in August 2005, a broad cross-section of Merced residents have expressed their concerns related to local and regional air quality impacts from this project. In January 2007, MMCAC members voted to formally oppose the project. We believed then that the project's negative impacts to the health and quality of life of Valley and local residents outweighed its employment benefits. **We still have serious concerns that the negative consequences of the project on local residents most affected by the project's impacts 1) are not adequately addressed and 2) are not adequately reduced to a less than significant level.**

17-1

Put simply, we submit these comments because the health of our members and our community is directly affected by the project.

The most recent California Health Interview Survey (CHIS) shows that out of 51,000 Merced County residents diagnosed with asthma, 17,000 are children. In 2006, over 700 children visited local Emergency Rooms due to asthma-related illnesses. In 2007, at least two Merced County residents died from asthma attacks (one pregnant, single mother in the City of Merced and one mother in Los Banos). A recent study by Cal State Fullerton Professor Jane Hall estimated that the public would save $5.8 billion in health costs if air pollution in the San Joaquin Valley met federal health-based standards. We must do everything in our power, and we ask you to do the same, to ensure Merced County residents, especially children, are able to live, learn and grow up in a healthy environment, which is why we oppose the proposed Wal-Mart Distribution Center.

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Air pollution is the number one environmental concern for the people of the Valley. It endangers the health of residents, retards the growth of crops, and threatens the overall economy and quality of life in the region. The economic benefits of the project should be studied and weighed against the economic costs of its air quality impacts. As stated, we oppose the proposed WMDC due to both the negative consequences to residents' health and the burden that will be placed on the economy if 100% of the pollution generated by the proposed project is not fully mitigated through proactive measures (locally and regionally).

We have three main areas of concern:

1. Assumptions made in the Draft Environmental Impact Review (DEIR) are based on confusing and dubious studies.
2. The DEIR does not "identify and discuss all feasible measures that will reduce air quality impacts generated by the project," as requested by the Air District in their Notice of Preparation letter and as required by CEQA.
3. The full extent of the Valley's air quality public health crisis has not been taken into account on all levels of planning.

17-2

*The DEIR's underlying analysis is flawed and inadequate.*

Despite the many pages of technical writing included in the DEIR, we are left with a number of questions. We feel that the urgent reality our members experience in Merced County classrooms, living rooms and emergency rooms is not adequately reflected in this document. Without a reliable set of studies, we question the adequacy of any subsequent mitigation measures, permitting actions, or voluntary agreement.

17-3

There are fundamental questions that still need to be answered.

***How many trucks precisely will use the facility?***

The WMDC's Notice of Preparation released July 7, 2006, states that "The project is expected to accommodate up to 900 tractor/trailer trips per day (450 in and 450 out)." However, there is no reference to this number, nor does the DEIR at any point make reference to a maximum peak hour number of truck trips. Instead, the authors of the studies rely on an e-mail communication from Lynn McAlexander, Wal-Mart's former Project Manager for Distribution Center Design. McAlexander's e-mail apparently states that Wal-Mart's distribution center in Apple Valley generates an average of 644 truck trips per day.

A rough daily average of 644 truck trips does not preclude a maximum of 900 truck trips in a day – an additional 28.5% truck trips. This alone renders the 2010 and 2030 traffic studies and subsequent mitigation measures flawed and virtually useless as a document to be used as the basis for such an important decision.

17-4

- What would the project's impact be if the traffic study studied the actual PM Peak Hour traffic with the project? What further mitigation would be required if the actual number of PM Peak Hour trucks were studied? If the suggested mitigation is inadequate for actual PM Peak Hour traffic, what will happen?
- How many more idling trucks would sit at the intersection? How long would the trucks wait for the stoplight to change? How much more carcinogenic diesel soot would students, teachers and staff breathe?

17-5

- Will traffic back up onto SR 99? If traffic backs up, or if the Mission and SR 99 intersection becomes known as a problematic intersection, what other routes will trucks use to avoid it? 17-6

These, or similar questions can be asked of each intersection that the traffic analysis claims to study. The studies that depend on a rough estimate of truck trips should be redone to include a peak hour number of maximum truck trips, their associated emissions and further mitigation measures. These new studies should not be speculative; they should instead provide an accurate assessment of impacts to an already overburdened neighborhood. 17-7

***Where will trucks using the Merced WMDC travel to and from?***

The DEIR's measurement of truck trips is internally inconsistent and appears to avoid a good faith effort at full disclosure of impacts to Air Districts outside the San Joaquin Valley.

The DEIR again bases its operational emission estimates on an e-mail from former Wal-Mart Project Manager for Distribution Center Design Lynn McAlexander. According to McAlexander's data for trip distances for the proposed project:

| | **Operation-related emissions of criteria air pollutants and precursors** | **Operation-related emissions of carbon dioxide** |
|---|---|---|
| **Average inbound receivable truck trip distance** | **106.2 miles/trip** "in the San Joaquin Valley Air Basin" between the 49 existing Wal-Mart stores and existing DC in Red Bluff or Porterville | **171.5 miles/trip** "in *and beyond* the San Joaquin Valley Air Basin" between 49 existing Wal-Mart stores and existing DC in Red Bluff or Porterville |
| **Average outbound delivery truck trip distance** | **83 miles/trip** "in the San Joaquin Valley Air Basin" to the 49 existing Wal-Mart stores | **109.1 miles/trip** "in *and beyond* the San Joaquin Valley Air Basin" to the 49 existing Wal-Mart stores |

17-8

We note that Table 4.2-7 shows a stunning amount of existing operational emissions contributing to criteria air pollutants. Wal-Mart's truck traffic that would travel to 49 existing stores, which would be supplied by the Merced WMDC, will be responsible for **343 tons/year of NOx and 207 tons/year of PM10.**

We need more information about three assumptions made in the DEIR's operational emissions study.

1. The DEIR measures trip distance outside the San Joaquin Valley Air Basin when determining CO2 emissions, but not for criteria air pollutants. If the trucks travel outside the San Joaquin Valley Air Basin then the DEIR should a) state the attainment status of each Air District, b) estimate the amount of emissions that will pollute each Air Basin as a result of this project, and c) contact each Air Basin for comment. Any change in truck route from the Port of Oakland should be studied as well. 17-9

2. In order to understand how many miles trucks using the Merced WMDC would actually travel, we would need to know which stores the distribution center is intended to serve. Please provide a list of the 49 existing stores in the San Joaquin Valley Air Basin upon which the DEIR's traffic studies are based. 17-10

3. It is unclear why Inbound Receivable net emissions total precisely 0.0 TPY of all criteria air pollutants and precursors. Even if all trucks using the Merced WMDC were already delivering goods to the supposed 49 existing stores in the San Joaquin Valley Air Basin, the trucks still need to travel over 1 mile from SR 99 to the Gerard Ave. entrance. These emissions must be acknowledged, assessed and appropriately mitigated. 17-11

***A full Health Risk Assessment needs to be conducted by trained Air District staff with community input.***

**We call for a full Health Risk Assessment (HRA) to be completed with specific attention paid to the local area "sensitive sites" (Farmdale Elementary School, Pioneer Elementary School and Weaver Middle School as well as the proposed school site in the area).**

In order to adequately understand the health impacts introduced by the project, a full Health Risk Assessment that includes a study of cancer risk caused by off-site WMDC project traffic should be conducted. The 7.3 in 1 million elevated cancer risk should not be dismissed as insignificant. The DEIR should include concrete measures that will be taken to reduce this cancer risk to a minimum. as low as feasible. 17-12

In order to assess the actual cancer risk introduced by this project, two additional sources of emissions should be included:

1) Off-site traffic-related emissions generated by the project should be included. The proposed truck route passes within approximately 1,000 feet from Pioneer Elementary school and appears to be adjacent to a planned Weaver School District elementary school site between Childs Ave. and Gerard Ave.

2) A thorough HRA, one that allows residents to understand the health risks posed to our community by this project, would include a study of sensitive receptors' exposure to Toxic Air Contaminants from 2030 traffic conditions projected to come about with the project.

We note that the project is less than half of the Heavy Industrial zoned land in southeast Merced that was added to the City in 1997 as part of the Lyons Annexation. Other proposed industrial uses in the Annexation area include a 350 megawatt peaking power plant and an industrial park on the eastern side of Kibby and Childs Ave. The traffic study ignores the build-out of these uses and the cumulative health impacts of all proposed projects. 17-13

***The Public must be involved in the Air Impact Assessment, Rule 9510 and voluntary emissions reduction agreement***

The Coalition has several concerns about the Air Impact Assessment process as described in the DEIR. The MMCAC requests to participate and consult with the San Joaquin Valley Unified Air Pollution Control District (SJVUAPCD) as local stakeholders and experts on any voluntary agreement between Wal-Mart and the SJVUAPCD. 17-14

Any agreement between Wal-Mart and the SJVUAPCD should be noticed and circulated for public review and given ample time for comment by the public and relevant agencies. Specific details regarding *how* mitigation is performed and monitored are a critical component of the decision-making process. Simply stating that at some point in the future, dozens of tons per year of criteria air pollutants will be mitigated is inadequate and inappropriately defers mitigation. Because we live in one of the country's most polluted air basins with four times the National asthma rates, it is absolutely critical that mitigation happen immediately (locally and regionally). 17-14 Cont'd

The MMCAC encourages the use of on-site mitigation that reduces actual emissions from vehicles entering and exiting the Merced WMDC. 17-15

**A majority of trucks using the Merced WMDC would be non-Wal-Mart trucks. We encourage the development of an enforceable mitigation program that monitors *all* trucks using the facility.** 17-16

Indirect Source Review (ISR) compliance and any voluntary agreement should consider that the Merced WMDC, if approved, would operate in Merced for decades. For example, an off-site in-lieu fee used to replace an agricultural pump with a seven- year lifespan is not an adequate mitigation measure in itself. **The SJVUAPCD should require Wal-Mart to mitigate each type of criteria pollutant to zero for the life of the project.**

The DEIR's claim that the SJVUAPCD "has not identified mass emissions thresholds for operational emissions of PM10 and PM2.5" is disputable. MMCAC members participated in the SJVUAPCD's process for writing the strongest possible State Implementation Plan (SIP) for attaining health protective fine particulate standards. Even assuming that the DEIR's estimate of 16.5 TPY of PM10 after ISR mitigation is accurate, it is inappropriate and dangerous to state that this is not worth mitigating. 17-17

**Given the extreme air quality public health crisis that our members experience on a daily basis, the SJVUAPCD should require 2:1 mitigation per ton of pollutant.** 17-18

If the City of Merced is going to monitor the voluntary agreement mitigation measures, we ask that the SJVUAPCD and California Air Resources Board (CARB) staff train City of Merced staff in appropriate fields to assist in gaining expertise in recognizing and mitigating criteria pollutants.

One such field could be training City public services staff to inspect heavy duty diesel trucks for proper tags, compliance with idling regulations, etc. MMCAC members could be available to train City of Merced staff in indoor and outdoor air quality conditions and related areas. 17-19

Finally, we again emphasize that localized coarse, fine and ultrafine PM emissions must be fully accounted for and reduced to the maximum extent possible using the Best Available Control Technology (BACT). **If Wal-Mart chooses to pay an in-lieu fee, we request 1) that PM emissions be mitigated at a 2:1 ratio and 2) that on-site fees be directed towards helping Merced residents cope with the real world health impacts of local PM emissions.** 17-20

The DEIR should also discuss how this project may interfere with regional or countywide emission reduction goals set under SB 375. These goals should be included in the City of Merced's updated General Plan. 17-21

The City of Merced has been in the process of updating its General Plan for nearly two years. The current City of Merced Vision 2015 General Plan, written in 1995-6 and approved in 1997, is out-of-date. The City is out of compliance with the letter and intent of AB 170. This project contradicts the "Toxic and Hazardous Emissions" section of the SJVAPCD's *Air Quality Guidelines for General Plans*. 17-22

As stated in the DEIR, Wal-Mart intends to "take advantage of the local labor force". As a good-faith commitment and in order to reduce the Vehicle Miles Traveled (VMTs) as required by SB 375, the Wal-Mart Corporation must hire 90% of all WMDC employees from Merced County (residents who live in Merced County prior to employment). Specific attention should be paid to Merced County's unemployed. If training is required for new employees, then the Wal-Mart Corporation must implement a training program that will educate the majority of the unemployed labor force in Merced County on the basics of the job and how to do it. 17-23

Wal-Mart must also pay for and provide alternative modes of transportation for its employees, such as:

- Purchasing carpool vehicles to create WMDC's "Carless Commute" which would serve employees and the various shifts
- Providing on-site services such as postal, banking services and showers for bicycle commuters
- Providing and encouraging "Bike-to-Work" days, weeks, seasons, etc.
- Installing one state-of-the-art bike locker for every 20 employees

As discussed, the MMCAC supports full mitigation of project impacts in a manner that corresponds to the project's real world health impacts. Any voluntary agreement between Wal-Mart and the SJVUAPCD should prioritize on-site measures that reduce the project's air pollutants to a less than significant level.

For example:

- No truck with an engine older than 2007 Model Year (MY) will be permitted to use the facility. Wal-Mart staff will be required to submit monthly reports to City staff detailing the model year of the trucks entering the facility.
- A fund will be created to retrofit or replace the trucks that will enter the project site.
- As a good-faith measure, Wal-Mart will need to purchase at least two PM2.5 forecasting monitors to assist the SJVUAPCD in "improving the health and quality of life for all Valley residents through effective and cooperative air quality programs". 17-24

If these are determined to be somehow infeasible or unacceptable, we request that funds be directed to specific programs that create a healthier and more livable community for Merced residents directly affected by the project's impacts.
For example:

- Funds designated to hire three full-time nurses to staff Weaver and Pioneer schools and administer a program that will help students live a healthy and successful life even in the most polluted air basin in the U.S.
- Funds designated to staffing the urgent care facility in Mercy Hospital as well as training and hiring additional respiratory therapists.
- Funds designated to assist southeast Merced residents in purchasing asthma equipment such as inhalers and spacers.

- Funds designated to build publicly-owned infrastructure in southeast Merced that encourages healthy exercise and community building. This could include a Community Center with the most efficient, state-of-the-art Heating Ventilating Air Conditioning (HVAC) system.
- Funds designated to the Weaver School District to offset the cost of the site selection process of a new school site.
- Funds to plant a perimeter of redwood, deodar cedar trees, and/or broad-leaf live oaks around the 1.1 Million Sq. Ft. property and along the project truck route. These types of trees are "highly effective in filtering some of the most toxic particles in auto exhaust." (Sacbee / News: Published May 6, 2008)
- Merced needs to move towards becoming more "green", not "green washing" as Wal-Mart seems to do. We need to be at the fore front of the green movement not lag behind. All of the green issues with Wal-Mart need to be resolved before it moves forward.
- Wal-Mart should pay for the entire cost for all asthma, heart disease, allergy and cancer treatment and medication for residents living within a two mile radius of the proposed Wal-Mart Distribution Center who are diagnosed with the listed diseases or ailments if diagnosis is given on or after the start of WMDC construction.
- As Wal-Mart actively pursues community involvement, we request a management representative from Wal-Mart be required to join the Merced/Mariposa County Asthma Coalition with 80%attendance/annually of all meetings.
- In addition, Wal-Mart needs to be required to fly the Asthma-Friendly Air Quality flags in front of their building and provide mandatory staff presentations explaining the importance of the flag program and asthma education. The Merced/Mariposa County Asthma Coalition will be available to provide the staff presentations.

17-24 Cont'd

Any mitigation measures as a result of this project should be binding with a clear timetable for implementation and benchmarks to measure their success.

17-25

A measure stating that "the project shall include as many clean alternative energy features as possible to promote energy self-sufficiency" (2-17) is too vague. Please note, natural gas is not the Best Available Technology for alternative energy and will also create a more localized, cumulative air pollution burden on the area.

Mitigation Measure 4.2-2d states that "If, however, the additional measures listed below are technologically or economically infeasible, the Applicant shall submit a written report to the City of Merced Planning & Permitting demonstrating such infeasibility. Approval of this report shall be received by the Applicant prior to receiving final discretionary approval of the project from the City of Merced Planning & Permitting."

17-26

We request that 1) if Wal-Mart submits such a written report it be made available for public review and a reasonable amount of time be given to comment on such a report (30 days minimum), and 2) that knowledgeable independent experts determine whether additional measures are truly technologically or economically infeasible.

Thank you for taking our comments and recommendations seriously. As stated above, the Merced/Mariposa County Asthma Coalition adamantly opposes the proposed Wal-Mart Distribution Center due to the negative health impacts the project will create. As the process moves forward, we urge the City to make the process as open, inclusive and accessible as possible to all Merced residents. We have full confidence that if the City of Merced chooses to move forward and approve the project,

that the recommendations above will be implemented into an agreement between the City of Merced (its residents) and the Wal-Mart Corporation.

Please contact us if you have any questions.

Sincerely,

Connie Mull, RN
Chair

Attachments:


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## Original Contribution

# Association of Black Carbon with Cognition among Children in a Prospective Birth Cohort Study

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While studies show that ultrafine and fine particles can be translocated from the lungs to the central nervous system, the possible neurodegenerative effect of air pollution remains largely unexplored. The authors examined the relation between black carbon, a marker for traffic particles, and cognition among 202 Boston, Massachusetts, children (mean age = 9.7 years (standard deviation, 1.7)) in a prospective birth cohort study (1986–2001). Local black carbon levels were estimated using a validated spatiotemporal land-use regression model (mean predicted annual black carbon level, 0.56 μg/m$^3$ (standard deviation, 0.13)). The Wide Range Assessment of Memory and Learning and the Kaufman Brief Intelligence Test were administered for assessment of cognitive constructs. In analysis adjusting for sociodemographic factors, birth weight, blood lead level, and tobacco smoke exposure, black carbon (per interquartile-range increase) was associated with decreases in the vocabulary (−2.2, 95% confidence interval (CI): −5.5, 1.1), matrices (−4.0, 95% CI: −7.6, −0.5), and composite intelligence quotient (−3.4, 95% CI: −6.6, −0.3) scores of the Kaufman Brief Intelligence Test and with decreases on the visual subscale (−5.4, 95% CI: −8.9, −1.9) and general index (−3.9, 95% CI: −7.5, −0.3) of the Wide Range Assessment of Memory and Learning. Higher levels of black carbon predicted decreased cognitive function across assessments of verbal and nonverbal intelligence and memory constructs.

air pollution; child; cognition; intelligence; neurotoxicity syndromes; particulate matter; soot; vehicle emissions

Abbreviations: CI, confidence interval; IQ, intelligence quotient; K-BIT, Kaufman Brief Intelligence Test; SD, standard deviation; WRAML, Wide Range Assessment of Memory and Learning.

It is well documented that air pollution is associated with a number of adverse respiratory and cardiovascular health effects (1–3). Many of these effects seem to be more strongly associated with particles from traffic (1), which are rich in elemental carbon and are the principal source of ultrafine particle exposure. However, the possible neurodegenerative effect of air pollution remains largely unexplored. The potential effect of translocation of particles from the lung to other organs has been documented. Researchers have shown that ultrafine and fine particles can be translocated from the lungs when they penetrate pulmonary tissue and enter the capillaries, reaching other organs (i.e., liver, spleen, kidneys, heart, brain) through circulation (4). In addition, fine and coarse particles can be phagocytized by macrophages and dendritic cells carrying the particles to the lymph nodes (5).

Animal studies have shown that inhaled particles can be translocated from the respiratory system directly to the central nervous system. In rats, Oberdorster et al. (6) found ultrafine carbon-13 particles in the olfactory bulb and the

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cerebrum and cerebellum after inhalation exposure of ultrafine elemental carbon-13 particles. More recently, Elder et al. (4) confirmed that ultrafine particles can reach the brain, either through circulation or directly translocated to the olfactory nerve from the nose to the brain. This raises the question of whether traffic particles can have neurotoxic effects.

The few studies that have focused on the potentially neurotoxic effects of particulate matter have focused on pathologic lesions that are generally present in neurodegenerative diseases (i.e., Parkinson's disease and Alzheimer's disease). Researchers have proposed that damage mediated by the particles is probably related to the oxidative stress pathway. Calderón-Garcidueñas et al. (7) presented histologic evidence of chronic brain inflammation (i.e., nuclear factor-κB activation and inducible nitric oxide synthase production) and an acceleration of Alzheimer-like pathology (i.e., apoptotic glial white matter cells, nonneuritic plaques, neurofibrillary tangles) among canines chronically exposed to high levels of air pollutants in Mexico City. Levels of proinflammatory cytokines, including interleukin-1α and tumor necrosis factor-α, were higher in the brain tissues of mice exposed to particulate matter than in mice that were not exposed (8). In humans, exposure to severe air pollution has been associated with increased levels of cyclooxygenase-2, an inflammatory mediator, and accumulation of the 42-amino-acid form of β-amyloid, a cause of neuronal dysfunction (9). Changes in brain cytokine and chemokine expression in mice have been directly linked to intranasal exposure to ultrafine black carbon, suggesting a more general inflammatory response (10). Changes in cognitive function have been shown to be associated with relatively low doses of heavy metal exposure (11), which in high doses can produce some of the lesions cited above. Those low doses have also been associated with increased inflammation and oxidative stress.

Taken together, these results suggested that further examination of possible associations between markers of traffic particles and cognitive function would be worthwhile. Thus, we examined the relation between black carbon from traffic sources, a component of particulate matter, and cognition among children followed in a prospective birth cohort study. This provided us with the opportunity to adjust for markers of socioeconomic status and other environmental factors known to affect cognitive development.

## MATERIALS AND METHODS

### Study population

The sample for these analyses was drawn from participants in the Maternal-Infant Smoking Study of East Boston, a prospective cohort study designed to evaluate the effects of pre- and postnatal tobacco smoke exposure on childhood lung growth and development and respiratory health. The study has been described in detail previously (12). In brief, pregnant women receiving prenatal care (<20th week of gestation) at an urban community health center in Boston, Massachusetts, between March 1986 and October 1992 were eligible for enrollment. Women who did not speak either English or Spanish, who did not plan to have pediatric follow-up at the clinic, and who were less than 18 years of age at the time were excluded. One thousand women were eligible and enrolled, of whom 848 continued participation and delivered a live infant. In November 1996, new study initiatives were implemented, including the assessment of social stressors and neurocognitive assessment, at which time 500 women and their children continued active follow-up. All active subjects were approached to participate in the cognitive battery, and 218 children completed the neurocognitive assessment. Notably, there were no significant differences between those who participated in the cognitive assessment and those who did not with regard to sociodemographic factors, birth weight, blood lead level, or tobacco smoke exposure. The study was approved by the human studies committees at the Harvard School of Public Health, Brigham and Women's Hospital, and the Beth Israel Deaconess Medical Center.

In the longitudinal study, detailed data on race/ethnicity and socioeconomic position (based on maternal educational level) had been ascertained through standardized questionnaires administered at baseline and clinic follow-up visits, as previously described (12).

### Black carbon

Exposure to black carbon was estimated on the basis of the children's residence during study follow-up. In order to estimate residential black carbon level, we used a validated spatiotemporal land-use regression model to predict 24-hour measures of traffic exposure using data from more than 80 locations in the Greater Boston area. Three quarters of the monitoring sites were residential; the rest were commercial or government facilities. The data consisted of over 6,021 pollution measurements from 2,127 unique exposure days. A detailed description of all sources of exposure data is provided elsewhere (13). Predictors included in the regression analysis were the black carbon level at a central stationary monitor (to capture average concentrations in the area on that day), meteorologic conditions and other characteristics (e.g., weekday/weekend) of a particular day, and measures of the amount of traffic activity (e.g., geographic-information-system-based measures of cumulative traffic density within 100 m, population density, distance to the nearest major roadway, percentage of urbanization) at a given location. A cumulative traffic density measure was recorded once per location. We used spline regression methods to allow these factors to affect exposure levels in a potentially nonlinear way. Finally, we used thin-plate splines, a two-dimensional extension of regression splines, to model longitude and latitude and capture additional spatial variability that was unaccounted for after we included our deterministic spatial predictors in the model. This approach is a form of universal kriging (i.e., kriging extended to incorporate covariates) or a geoadditive model (14) for daily concentrations of particle levels. We had complete information on all of these factors for 2,114 of the 2,127 unique exposure days. Separate models were fitted for the warm (May–October) and cold (November–April) seasons. The $R^2$ value for the model (over both seasons) was 0.82, and the cross-validated $R^2$ between the daily measurements

taken outside the residential locations and corresponding predictions obtained from fitting the model to the data after excluding data from a particular residential location was 0.36. For the purposes of these analyses, we used the average of the two seasons as a measure of average lifetime black carbon exposure. If children moved during the study period ($n = 12$), an average black carbon measure for all addresses was calculated.

### Cognitive measures

When the children were aged 8–11 years, a battery of cognitive tests was administered, including the Kaufman Brief Intelligence Test (K-BIT) and the Wide Range Assessment of Memory and Learning (WRAML). The K-BIT is an individually administered test of verbal and nonverbal intelligence (15). Two subscales, vocabulary and matrices, comprise the test, as well as a composite intelligence quotient (IQ) score. The K-BIT has acceptable correlation with the widely used Wechsler verbal performance and full-scale IQ scores (16); validation studies have been conducted for children less than 7 years of age with normative data available (17). The WRAML is a well-standardized psychometric instrument that allows evaluation of a child's ability to actively learn and memorize a variety of information (18, 19). The WRAML includes subscales on verbal memory, visual memory, and learning and an overall general index scale. It has been normed for children aged 5–17 years among racially diverse groups, including minorities. All measures are expressed as standardized scores, which represent the score of the individual taking the test relative to scores obtained by children of the same age and gender in the standardization sample. All scores have a mean of 100 and a standard deviation of 15.

### Tobacco smoke exposure

At each clinic visit during pregnancy, mothers were asked about their smoking status and the smoking habits of members of their households. A urine specimen was obtained for determination of a creatinine-corrected cotinine level, as previously detailed (12). A mother was classified as never smoking during her pregnancy if she always reported that she had never smoked on the standardized questionnaire and each of her urinary cotinine levels was less than 200 ng/mg creatinine (12). At any visit, if the report of nonsmoking by the mother was contradicted by the urinary cotinine measure, the mother was classified as a current smoker for that interval. Maternally reported postnatal exposure of the child to secondhand smoke was assessed by questionnaire (monthly through age 26 months, every 6 months between ages 26 months and 4 years, and annually thereafter). Children were considered to have been exposed to secondhand smoke in a particular follow-up interval if the mother reported personal active smoking or active smoking by any other person living in the household. Postnatal secondhand smoke was categorized as early (occurring from birth through 25 months of age) or late (26 months of age or older). The late secondhand smoke exposure category included children exposed both early and late (54 children) and late only (13 children), given that there were relatively few children in the latter category. Children's exposure to maternal smoking during pregnancy was highly correlated with postnatal secondhand smoke exposure. Forty-two children were exposed to prenatal tobacco smoke; among these children, only two were not exposed to secondhand smoke after birth.

### Blood lead level

Children in Massachusetts are mandated by law to have blood lead testing annually, starting at 9 months of age, until age 4 years, unless they are considered to be at high risk (living in pre-1978 housing that is deteriorated or undergoing construction or having a sibling with lead poisoning), in which case they are tested annually until age 6 years. Results are incorporated into the medical records at the community health centers where the children obtain pediatric follow-up. Using a standardized instrument, blood lead levels were extracted from medical records at these health centers by a physician blinded to the study aims. Because the children had varying numbers of blood lead measurements which were dependent on their lead exposure (children with higher lead exposure had more follow-up tests than children with lower lead concentrations), we used the highest blood lead level recorded up to age 6 years for each child, referred to hereafter as the "peak blood lead level."

### Statistical analyses

A total of 218 children completed the cognitive assessment, of whom 214 were successfully geocoded and assigned a black carbon measure. Eleven children were removed from the data set before analysis because they had black carbon values considered to be outliers according to the extreme studentized deviation model (20); in addition, one child was missing information on socioeconomic status. This left 202 children for our analyses. Multiple imputation was used to impute missing data on birth weight (seven children) and blood lead level (12 children). Since black carbon was being used as a surrogate for traffic particle exposure, which includes more than just carbon particles, it did not make sense for us to report results on a unit mass basis. Instead, we report estimated effects of predicted black carbon level per interquartile-range increase. We conducted bivariate analyses to determine the association between cognitive outcomes and demographic and environmental measures of interest. We also tested for associations between black carbon and environmental and sociodemographic markers. The effect of predicted black carbon on cognition was estimated by linear regression while adjusting for child's age at cognitive assessment, gender, race/ethnicity, and maternal education (as a marker of socioeconomic status) (model 1). To assess the potential for confounding, we examined the sensitivity of those results to further adjustment for in-utero and postnatal secondhand tobacco smoke exposure (model 2), birth weight (model 3), and blood lead level (model 4). All analyses were conducted in SAS, version 9.0 (SAS Institute, Inc., Cary, North Carolina).

## RESULTS

Among the 202 children in this study, 52 percent were female and 57 percent spoke Spanish as their primary language. Maternal educational level was less than high school graduation for 42 percent of the mothers (table 1). The mean age was 9.7 years (standard deviation (SD), 1.7), and the mean peak blood lead level was 8.5 μg/dl (SD, 6.1). Mean scores on the K-BIT subscales were as follows: composite, 94.9 (SD, 13.9); vocabulary, 89.5 (SD, 16.3); and matrices, 101.4 (SD, 14.0). WRAML mean subscale scores were: verbal memory index, 84.7 (SD, 15.1); visual memory index, 93.3 (SD, 13.8); learning index, 101.1 (SD, 15.0); and general index, 91.1 (SD, 14.5). The mean annual predicted black carbon level was 0.56 $\mu g/m^3$ (SD, 0.13).

In bivariate analyses (data not shown) of black carbon and cognitive measures, black carbon was associated with the vocabulary, matrices, and composite subscales of the K-BIT and the visual and verbal subscales and the general index of the WRAML. Primary language spoken at home and maternal education were associated with the cognitive measures and black carbon. Children who primarily spoke Spanish at home and children whose parents had a high school education or less scored lower on the composite, vocabulary, verbal, and general memory subscales of the WRAML and K-BIT. In addition, they had higher predicted black carbon levels than children who primarily spoke English at home and whose parents had more than a high school education. Marital status was not associated with any of the cognitive measures or with black carbon. Thus, in multivariate analyses, we adjusted for both parental education and primary language spoken at home, as well as birth weight, blood lead level, and in-utero and postnatal secondhand tobacco smoke exposure.

In multiple linear regression analyses (tables 2 and 3), an interquartile-range increase in log black carbon predicted a 2-point decrease (95 percent confidence interval (CI): −5.3, 1.3) on the vocabulary scale, a 4.2-point decrease (95 percent CI: −7.7, −0.7) on the matrices scale, and a 3.4-point decrease (95 percent CI: −6.6, −0.3) on the composite subscale of the K-BIT. Black carbon level also predicted a 1.1-point decrease (95 percent CI: −4.6, 2.3) on the verbal learning scale, a 5.2-point decrease (95 percent CI: −8.6, 1.7) on the visual learning scale, a 2.7-point decrease (95 percent CI: −6.5, 1.1) on the learning scale, and a 3.7-point decrease (95 percent CI: −7.2, −0.2) on the general index scale of the WRAML. Further adjustment for tobacco smoke exposure, birth weight, and blood lead level did not attenuate these effect estimates.

**TABLE 1. Demographic characteristics, environmental exposures, and scores on cognitive subscale measures ($n = 202$) in the Maternal-Infant Smoking Study of East Boston, 1986–2001**

| | No. | % | Mean (SD*) |
|---|---|---|---|
| Demographic characteristics | | | |
| Child's age (years) | | | 9.7 (1.7) |
| Child's gender | | | |
| Male | 97 | 48.0 | |
| Female | 105 | 52.0 | |
| Primary language spoken at home | | | |
| English | 87 | 43.1 | |
| Spanish | 115 | 56.9 | |
| Mother's educational level | | | |
| Some college | 37 | 18.3 | |
| High school graduation/technical school | 81 | 40.1 | |
| Less than high school/no graduation | 84 | 41.6 | |
| Marital status | | | |
| Married/living with someone | 155 | 76.7 | |
| Separated/divorced/single | 47 | 23.3 | |
| Medical history and environmental exposures | | | |
| Tobacco exposure | | | |
| Nonsmoker | 70 | 34.7 | |
| In-utero and SHS* exposure | 42 | 20.8 | |
| Early SHS exposure† | 23 | 11.4 | |
| Late SHS exposure‡ | 67 | 33.2 | |
| Birth weight (kg) | | | 3.35 (0.5) |
| Peak blood lead level (μg/dl) | | | 8.5 (6.1) |
| Black carbon ($\mu g/m^3$) | | | 0.56 (0.13) |
| Cognitive subscales | | | |
| Kaufman Brief Intelligence Test | | | |
| Composite | | | 94.9 (13.9) |
| Matrices | | | 101.4 (14.0) |
| Vocabulary | | | 89.5 (16.3) |
| Wide Range Assessment of Memory and Learning | | | |
| Verbal | | | 84.7 (15.1) |
| Learning | | | 101.1 (15.0) |
| Visual | | | 93.3 (13.8) |
| General index | | | 91.1 (14.5) |

* SD, standard deviation; SHS, secondhand smoke.
† SHS exposure before 26 months of age.
‡ SHS exposure at 26 months of age or older.

## DISCUSSION

In this prospective urban birth cohort study, long-term concentration of black carbon particles from mobile sources was associated with decreases in cognitive test scores, even after adjustment for socioeconomic status, birth weight, tobacco smoke exposure, and blood lead level. Although our linear regression-based analyses do not establish causation, only associations, a number of features strengthen our findings. Decreases in cognitive functioning were seen in verbal and nonverbal intelligence constructs as well as memory constructs. Moreover, our results are consistent in that we noted decreases across all subscales, though not all associations between black carbon and cognitive subscales were statistically significant.

**TABLE 2. Relation of predicted black carbon levels (average of summer and winter) at children's residences to scores on subscales of the Kaufman Brief Intelligence Test in linear regression models ($n = 202$), Maternal Infant Smoking Study of East Boston, 1986–2001†**

| Black carbon model | Vocabulary | | Matrices | | Composite | |
|---|---|---|---|---|---|---|
| | Estimate | 95% CI‡ | Estimate | 95% CI | Estimate | 95% CI |
| Adjusted for demographic factors§ | −2.0 | −5.3, 1.3 | −4.2 | −7.7, −0.7* | −3.4 | −6.6, −0.3* |
| Adjusted for above factors + in-utero tobacco smoke + secondhand smoke | −2.0 | −5.3, 1.4 | −4.0 | −7.5, −0.4* | −3.3 | −6.4, −0.1* |
| Adjusted for above factors + birth weight | −2.0 | −5.4, 1.3 | −4.0 | −7.6, −0.5* | −3.3 | −6.5, −0.2* |
| Adjusted for above factors + blood lead level | −2.2 | −5.5, 1.1 | −4.0 | −7.6, −0.5* | −3.4 | −6.6, −0.3* |

* $p < 0.05$.
† Change in subscale score per interquartile-range (0.4-μg/m$^3$) increase in log black carbon level.
‡ CI, confidence interval.
§ Adjusted for age, gender, primary language spoken at home, and mother's education.

These results are of comparable magnitude to results found for other environmental neurotoxicants. For example, among children, a 10-μg/dl increase in blood lead level has been associated with a loss of 1–5 IQ points (21). Children born to mothers who smoke 10 or more cigarettes per day during pregnancy have an average decrease of 4 IQ points (22). In our cohort, an interquartile-range (0.4-μg/m$^3$) increase in log black carbon predicted a 3-point decrease in IQ (K-BIT composite subscale).

There are several potential mechanisms that could be contributing to the associations found in this study. First, since black carbon comes almost entirely from traffic, these particles are surrogates for all traffic particles, and other components of traffic particles may play a role. For example, there is evidence that ultrafine particles are translocated up the olfactory nerve to the brain without entering the lung (6). Ultrafine particles in the brain are probably associated with increased oxidative stress, since that has been seen in other tissues (23). The carbon particles themselves are rarely pure carbon; they generally have transition metals adsorbed on the surface. These metals have been shown to induce oxidative stress in the lung (24–28). Other studies have also implicated traffic exposure in oxidative stress (29–31). There is evidence that the oxidative stress and inflammation induced by particles translates systemically (30). For example, exposure of rodents to concentrated air particles collected from a busily trafficked roadway resulted in increased oxidative stress in the heart as well as the lung (31). Other studies comparing animal brains in areas of Mexico City that are heavily influenced by traffic have reported histologic evidence of chronic brain inflammation and an acceleration of Alzheimer-like pathology (7). Taken together, the current body of knowledge suggests that inflammatory processes and increased oxidative stress (7) may play a role in the mechanism by which particles can have an impact on the nervous system; however, additional work in this area of research remains to be done.

While, to our knowledge, no other studies have examined an association between air pollution and cognition, a few have examined the role of traffic noise in cognition among children (32, 33). In the RANCH project, a cross-sectional study of 2,000 children from three European cities (Madrid, London, and Amsterdam), aircraft noise at home and at school was associated with impaired reading comprehension (32). Road traffic noise, however, was not associated with reading comprehension. It is possible that the associations found in our study could be attributable to traffic and/or aircraft noise and not to black carbon; conversely, it is also possible that the associations previously found between road and aircraft noise and cognition are actually due to air

**TABLE 3. Relation of predicted black carbon levels (average of summer and winter) at children's residences to scores on subscales of the Wide Range Assessment of Memory and Learning in linear regression models ($n = 202$), Maternal Infant Smoking Study of East Boston, 1986–2001†**

| Black carbon model | Verbal | | Visual | | Learning | | General | |
|---|---|---|---|---|---|---|---|---|
| | Estimate | 95% CI‡ | Estimate | 95% CI | Estimate | 95% CI | Estimate | 95% CI |
| Adjusted for demographic factors§ | −1.1 | −4.6, 2.3 | −5.2 | −8.6, −1.7* | −2.7 | −6.5, 1.1 | −3.7 | −7.2, −0.2* |
| Adjusted for above factors + in-utero tobacco smoke + secondhand smoke | −1.2 | −4.7, 2.3 | −5.3 | −8.8, −1.8* | −2.6 | −6.5, 1.2 | −3.7 | −7.3, −0.1* |
| Adjusted for above factors + birth weight | −1.3 | −4.7, 2.2 | −5.3 | −8.8, −1.8* | −2.6 | −6.5, 1.3 | −3.8 | −7.4, −0.2* |
| Adjusted for above factors + blood lead level | −1.3 | −4.8, 2.2 | −5.4 | −8.9, −1.9* | −2.8 | −6.6, 1.1 | −3.9 | −7.5, −0.3* |

* $p < 0.05$.
† Change in subscale score per interquartile-range (0.4-μg/m$^3$) increase in log black carbon level.
‡ CI, confidence interval.
§ Adjusted for age, gender, primary language spoken at home, and mother's education.

pollutants, such as black carbon. Future studies may be designed to distinguish traffic effects due to noise from those due to pollution.

The current study had a number of limitations. As is typical with longitudinal studies, there was a significant reduction in the sample available from the original cohort over time. The nonparticipation of some subjects from the longitudinal study may be seen as a limitation, although there were no differences based on race/ethnicity, maternal education, smoking status, birth weight, or blood lead level when we compared children who had cognition assessed with those who did not among the participants who remained in follow-up. Thus, this is unlikely to have influenced our findings. While we were able to adjust for a number of factors associated with cognition and air pollution, it is still possible that the associations found in this study could be attributable to unmeasured or residual confounding, perhaps most notably from socioeconomic status. Socioeconomic status has been shown to be a determinant of cognitive ability and achievement from early childhood through young adulthood (34, 35). Furthermore, socioeconomic status can determine whether a family lives in close proximity to roadways (36). In addition to adjusting for mother's educational level, the present study was somewhat restricted regarding socioeconomic status, given that all families were recruited from one neighborhood health center in Boston. This restricted the variability of income in this population, thereby reducing the potential for confounding.

Our measure of exposure was also subject to limitations. While we attempted to capture black carbon exposure from all residential addresses, it is possible that we potentially missed exposures incurred at school and/or other locations where children spend portions of their time. However, this potential misclassification of exposure was nondifferential with respect to the outcome, and thus it is unlikely to account for the associations found. Furthermore, compared with adults who work, children spend considerably longer periods of time at home or in the vicinity of their home. Furthermore, exposure studies using personal monitors indicate that home exposures are the most important in predicting personal exposure (37). While demonstrated in adults, time activity studies indicate that children spend more time at home and near home, making the finding relevant (38). Other studies (39) have shown that residential indoor concentrations of particulate matter of outdoor origin are highly correlated with outdoor concentrations. In another study (40), the personal exposures of the working spouses of persons with chronic illnesses have been shown to be highly correlated with their spouses' personal exposures. Taken together, we believe these studies indicate that personal exposures to ambient particles are driven primarily by exposures incurred at home. Moreover, we attempted to capture black carbon exposure from all residential addresses when children moved.

Another limitation of this study is the use of predicted exposure, rather than observed measurements taken outside the residences of the study participants. Since the latter approach is not practical in a large community-based study, we decided to use all available exposure data and advanced modeling approaches to predict the missing exposure at the residences of the participants. This is an approach that has become very popular in recent years. A potential statistical issue that arises when using spatial-temporal predictions of exposure rather than measured quantities is that predicted quantities are uncertain, and this could bias the resulting health effect estimates. In a previous study, Gryparis et al. (41) found that the use of predictions from spatial exposure models induces a Berkson-type measurement error. This results in unbiased parameter estimates for the association between the predicted exposure and the observed health outcome. However, the standard errors for the parameter of interest might be incorrect. In such a case, we would expect larger standard errors for the parameter of interest.

In summary, this is the first study to have found a consistent relation between exposure to black carbon and reduced neurocognitive functioning across a number of domains in urban, community-dwelling school-aged children. More studies are needed to explore the potentially neurotoxic effects of particulate matter, both to determine the possible impact on cognitive development among children and cognitive decline across the life cycle and to determine the potential contribution of air pollutants to the development and exacerbation of neurodegenerative diseases (i.e., Parkinson's disease, Alzheimer's disease).

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**Research | Children's Health**

# Ambient Ozone Concentrations Cause Increased Hospitalizations for Asthma in Children: An 18-Year Study in Southern California

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**Abstract**

**Background:** Asthma is the most important chronic disease of childhood. The U.S. Environmental Protection Agency has concluded that children with asthma continue to be susceptible to ozone-associated adverse effects on their disease.

**Objectives:** This study was designed to evaluate time trends in associations between declining warm-season $O_3$ concentrations and hospitalization for asthma in children.

**Methods:** We undertook an ecologic study of hospital discharges for asthma during the high $O_3$ seasons in California's South Coast Air Basin (SoCAB) in children who ranged in age from birth to 19 years from 1983 to 2000. We used standard association and causal statistical analysis methods. Hospital discharge data were obtained from the State of California ; air pollution data were obtained from the California Air Resources Board, and demographic data from the 1980, 1990, and 2000 U.S. Census. SoCAB was divided into 195 spatial grids, and quarterly average $O_3$, sulfur dioxide, particulate matter with aerodynamic diameter ≤ 10 μm, nitrogen dioxide, and carbon monoxide were assigned to each unit for 3-month periods along with demographic variables.

**Results:** $O_3$ was the only pollutant associated with increased hospital admissions over the study period. Inclusion of a variety of demographic and weather variables accounted for all of the non-$O_3$ temporal changes in hospitalizations. We found a time-independent, constant effect of ambient levels of $O_3$ and quarterly hospital discharge rates for asthma. We estimate that the average effect of a 10-ppb mean increase in any given mean quarterly 1-hr maximum $O_3$ over the 18-year median of 87.7 ppb was a 4.6% increase in the same quarterly outcome.

**Conclusions:** Our data indicate that at current levels of $O_3$ experienced in Southern California, $O_3$ contributes to an increased risk of hospitalization for children with asthma.

Key words: air pollution, asthma, children, epidemiology, ozone. *Environ Health Perspect* 116:1063–1070 (2008) . doi:10.1289/ehp.10497 available via *http://dx.doi.org/* [Online 6 March 2008]

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## Introduction

In terms of numbers, morbidity burden, and health care costs, asthma is the most important chronic disease of childhood, with estimated medical care costs over $1 billion in 2005 (Wang et al. 2005). Based on its recent review of data on ozone-related health effects, the U.S. Environmental Protection Agency (EPA) has once again concluded that children with asthma constitute a group that is susceptible to $O_3$-associated adverse effects on their disease (U.S. EPA 2006). Hospitalization and visits to emergency departments are major contributors to childhood asthma-related health care costs and account for approximately 12% of care costs for asthma in children 5–17 years of age (Wanget al. 2005). Despite the large number of studies on various asthma-related outcomes (symptoms, lung function) in relation to ambient $O_3$, there are relatively few studies on $O_3$-related hospital discharges and emergency department (ED) visits in children with asthma; and the results of these studies have not been consistent [U.S. EPA 2006 (Figures 7-8, 7-9)]. Moreover, these studies have been concerned with associations between pollutant exposures over a few days before hospital admission and over relatively short periods of calendar time.

Several studies illustrate findings based on short lag periods. White and colleagues (1994) reported that ED visits for asthma (1–16 years of age) to an Atlanta, Georgia, hospital increased by 37% on the 6 days in the summer of 1990 when the maximum 1-hr $O_3$ concentrations exceeded 110 ppb. A subsequent Atlanta-based ecologic study reported that Medicaid claims for hospital admissions for asthma decreased during the time of the 1996 Summer Olympic Games in parallel with reductions of ambient $O_3$ concentrations (Friedman et al. 2001). The decline in $O_3$ was attributed to the marked decline in city traffic during the games, but associations with other mobile source emissions were not evaluated in

the regression models. A third study from Atlanta for the summers of 1993–1995 found similar associations with ED visits, but these investigators could not separate effects due to particulate matter with aerodynamic diameter ≤ 10 μm ($PM_{10}$) (Tolbert et al. 2000). An approximate 33% increase in ED visits for childhood asthma was reported from eastern Canada on days when the 1-hr maximum exceeded 75 ppb over the years 1984–1992, an association that was independent of concentrations of sulfate and total suspended particulates (TSP) (Stieb et al. 1996). Data from Washington, DC; Mexico City, Mexico; and Madrid, Spain, support these findings of $O_3$-associated increases in ED visits, independent of pollens and $PM_{10}$ (Babin et al. 2007; Galan et al. 2003; Romieu et al. 1995).

In contrast to the above results, several relatively recent European studies have not found these associations. Data from the APHEA (Air Pollution and Health: A European Approach) study from the period 1986–1992 from Barcelona, Spain; Helsinki, Finland; Paris, France; and London, UK, failed to find any association between ED visits and ambient $O_3$ in children < 15 years of age (Sunyer et al. 1997). However, these results were based on $O_3$ concentrations throughout all months of the year. Similarly, a study in London, based on year-long data for 12 EDs over the years 1992–1994, also failed to find any association between ED visits and hospitalizations for asthma and ambient $O_3$ concentrations for children from birth to 14 years of age (Atkinson et al. 1999a, 1999b).

California's South Coast Air Basin (SoCAB) has some of the highest concentrations of $O_3$ in the U.S. [South Coast Air Quality Management District (SCAQMD) 2006] and will continue to be a major area of noncompliance under proposed new $O_3$ standards (U.S. EPA 2005). Mobile source emissions are the main source of precursors for $O_3$ generation (Fujita et al. 1992). Because $O_3$ and other pollutant levels, in general, have been declining over the past 25 years (SCAQMD 2003), this area offers an excellent opportunity to study the relation between warm-season ambient $O_3$ concentrations and hospitalizations for asthma in a large population that spans urban and rural areas. Therefore, we undertook an ecologic study of hospital discharges for asthma in children from 0 (birth) to 19 years of age over the period 1983–2000 in the SoCAB to evaluate the effect of population-level $O_3$ exposure on asthma-related hospital discharge over time. Our approach is based on conventional linear modeling with adjustment for temporal factors that could confound the causal effect of interest. Our approach has several novel features: *a*) We used a very flexible, data-adaptive model fitting program that is based on multiple cross-validations (van der Laan and Dudoit 2003); *b*) pollutants other than $O_3$ could enter our modeling at equivalent levels of complexity, as for $O_3$, and *c*) we used marginal structural models (MSM) to support the interpretation of population-level effects of $O_3$ on the outcomes (van der Laan and Robins 2002).

## Methods

***Study area.*** The study area was the portion of California's SoCAB covered by the grids shown in Figure 1. The 20,000-$km^2$ area extends from 34.6° latitude at its most northern reach to 33.2° latitudeat its most southern extent. It is bounded on the west by –118.9° longitude and the Pacific Ocean, and extends to –116.8° longitude at its eastern end. We selected this location because it contained many areas that consistently exceeded National Ambient Air Quality Standards for $O_3$ during the 1980–2000 study period (U.S. EPA 2000). Nonetheless, the area also experienced marked reductions in 1-hr and 8-hr maximum $O_3$ concentrations over this time.

***Ambient pollutant data and exposure methods.*** We estimated the population's exposure to $O_3$, nitrogen dioxide, sulfur dioxide, carbon monoxide, PM with aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$), and $PM_{10}$ from ambient air quality measurements obtained from a network of stations that began monitoring for most of the pollutants before 1980. The number and locations of air monitoring stations (Figure 1) varied over the study period. The number of stations with valid air quality data in or near the grid in a given year varied from 45 to 55 for $O_3$, 33 to 41 for $NO_2$, 28 to 39 for CO, and 9 to 56 for $PM_{10}$. We compiled quarterly average concentrations of the 1-hr daily maximum $O_3$ and 24-hr average $NO_2$, $SO_2$, and CO from hourly measurements of gases. We compiled quarterly average concentrations of the 24-hr average $PM_{10}$ and $PM_{2.5}$ from monthly averages of every sixth day $PM_{10}$ measurements and daily, every third day, and 2-week average $PM_{2.5}$ measurements (Blanchard and Tanenbaum 2005). The air quality data were complemented with quarterly average daily 1-hr minimum and 24-hr average temperature and relative humidity data obtained from the SoCAB and National Weather Service measurements (National Climatic Data Center, NOAA Satellite and Information Service: http://www.ncdc.noaa.gov/oa/ncdc.html).

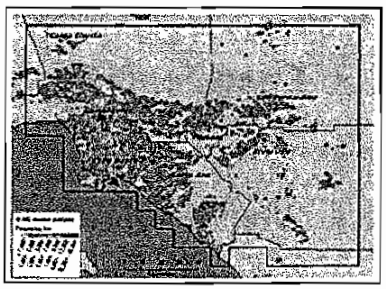
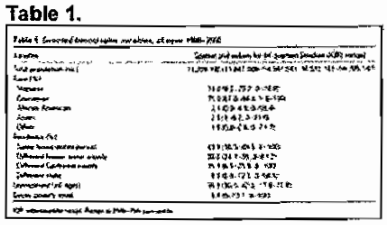


**Figure 1.** Study domain grid system with location of pollutant monitors and population density. AQ, air quality.

**Table 1.**



California $PM_{10}$ data are not widely available before 1988. Special study $PM_{10}$ mass data available in Burbank, downtown Los Angeles, Long Beach, Los Alamitos, Costa Mesa, Azusa, Rubidoux, Perris, and Banning were used for 1985–1987 (Solomon et al. 1988). Collocated $PM_{10}$ and TSP data for 1988 through 1992 in Los Angeles, Orange, San Bernardino, and Riverside Counties indicated that daily $PM_{10}$ concentrations were correlated with daily TSP and, on average, were 54% of TSP concentrations. The $PM_{10}$ concentrations for 1980–1984 were estimated from the TSP data based on this relation. $PM_{2.5}$ data were available for only 1994–2000.

The study domain was divided into two-hundred 10 km × 10 km spatial grids that covered the populated portion of the SoCAB, of which 195 were used. The population, other demographic, and health outcome data were aggregated into the grid cells [Supplemental Material, Figure S1 (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)]. The air quality and meteorologic data were interpolated spatially from the monitoring stations to the grid

cell centroids based on inverse distance-squared weighting. Maximum interpolation radii of 50 and 100 km were used for pollutants and meteorologic parameters, respectively. Although 100% of the grids had an $O_3$ air quality station within 50 km, 73% of the grids had a station within 5–25 km of the grid centroids and 13% of grids had a station located within the grid on average [see Supplemental Material (online at http://www.ehponline.org/members/2008/10497/suppl.pdf) for other pollutant interpolation distances]. This interpolation approach worked reasonably well in this application, because the spatial coverage in the SOCAB monitoring network is good (typically, stations located 20–30 km apart); and spatial gradients in monthly average concentrations are modest.

Our principal exposure of interest was 1-hr daily, maximum $O_3$. We chose this measure, because the same 1-hr maximum standard was in place for most of the study period; and the 1-hr maximum is the most commonly used metric in $O_3$ epidemiologic studies. Quarterly, average $O_3$ concentrations were low and showed little variability from October through March [see Supplemental Material, Figure S6 (online at http://www.ehponline.org/members/2008/10497/suppl.pdf) for sample quarters]. Therefore, we confined our analyses to April–June (quarter 2) and July–September (quarter 3), which constitute all months with the highest and most variable $O_3$ concentrations.

***Hospital discharge and demographic data.*** Since 1983, hospital discharges (diagnoses, demographic data and medical payments) have been reported semiannually by all hospitals licensed in California. Patient-level data were extracted from a CD-ROM (Healthcare Information Resource Center, Sacramento, CA) and included: patient age category, county of residence and 5-digit ZIP Code, ethnicity, sex, major diagnostic category (plus four secondary), major procedure (plus four secondary), quarter admitted, length of stay, and hospital ID number (Office of Statewide Health Planning and Development, data files e-mailed July 2003). We focused on quarterly hospital discharges for asthma [*International Classification of Diseases, 9th Revision* (ICD-9; World Health Organization 1975) code 493, ICD-10 (World Health Organization 1993) code J45/46] listed as the first discharge diagnosis for children and adolescents from birth through 19 years of age. We included discharges in which the first listed diagnoses were acute sinusitis (ICD-9 461; ICD-10 J01) or pneumonia (ICD-9 480–483, 485–487; ICD-10 J10–J18) and asthma was the second listed diagnosis, because we could not be sure of the extent to which the presence of asthma actually led to the hospitalization [see Supplemental Material (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)].

We obtained data from the U.S. Census Bureau's decadal surveys for years 1980, 1990, and 2000 [see Supplemental Material (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)]. We reviewed all income, demographic, and residential data and selected covariates that were considered likely to affect asthma morbidity and were likely to show spatial clustering and temporo-spatial trends (graphs available on request from authors). We selected 57 sociodemographic variables.

The finest spatial resolution for which hospital discharge data were available was the 5-digit postal ZIP code of the patient's residence; the patient's street address, 9-digit ZIP code, or census block were not available. Population-weighted ZIP-to-grid allocation factors were developed with geographic information system (GIS) tools for 1980–1984, 1995–1994, and 1995–2000. Separate allocations factors were developed for males and females for < 1 year and 1–19 years of age. [see Supplemental Material for details (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)].

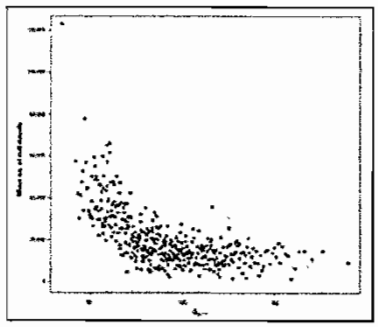


**Figure 2.** Distribution of population number by 400 quantiles of quarterly 1-hr maximum $O_3$ over quarters 2 and 3, 1983–2000.

**Table 2.**

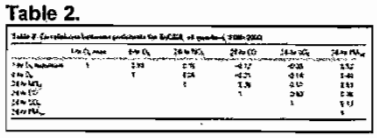
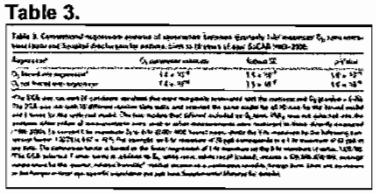


**Table 3.**



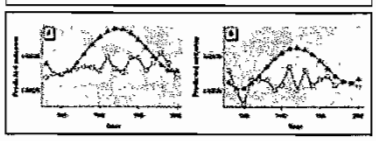
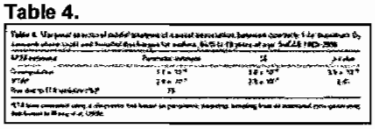


**Figure 3.** Predicted proportions of quarterly hospital discharges based on a model that included only time variables (triangles) and the model in Table 4 that includes $O_3$ and the demographic variables (squares) for quarters 2 (*A*) and 3 (*B*).

**Table 4.**



Spatial allocation of demographic data to exposure grids was based on the smallest geographic unit for which census data were available. We used GIS software (ArcGIS9; ESRI, Redlands, CA) to map the demographic data to grids. Eight population variables from 1980 and one population variable from 1990 and 2000 were renormalized after the spatial allocation to insure consistency across census topics (e.g., population by race was normalized by the total population; population by sex, age, and race was normalized for consistency with population by race and population by sex). Population and other demographic parameters were estimated for the intracensus years by linear interpolation of the gridded data for 1980, 1990, and 2000.

***Data analysis.*** **Data structure.** The data consist of 195 geographic units (grids) with quarterly measurements from 1983 through 2001 that include 14,040 records and 72 quarters for children birth to 19 years of age. We calculated the proportion of asthma-related hospital discharges as the number of asthma-related hospital discharges in each grid in each quarter divided by the total population birth to 19 years of age in the corresponding grid and quarter. After removal of nine outliers, we used data for quarters 2 and 3 only (7,011 observations).

There were no missing values for the proportion of asthma-related discharges or quarterly $O_3$. Among the 47 covariates considered, 35 had no missing values. Among the 12 remaining covariates, the proportion of missing values ranged from 0.4% to 6.2%.

**Statistical models.** We denote the observed data structure by $O = [W–(71), A–(71, Y–(72)]$ representing quarterly

measurements from time 0 to 72 of the confounders, $O_3$ levels and proportion of asthma-related hospital discharges: *a*) The history of $O_3$ is denoted by $A\text{–}(71) = [A(0),\ldots,A(71)]$, and $A(t)$ represents the $O_3$ level measured at time $t$; *b*) the history of asthma-related hospital discharges as a percentage of the total area-specific population is denoted by $Y\text{–}(72) = [Y(1), \ldots, Y(72)]$, and $Y(t)$ represents the proportion of asthma discharges measured at time $t$; and *c*) the history of potential time-dependent confounders of the effect of $O_3$ on asthma-related hospital discharges is denoted by $W\text{—}(K) = [W(0),\ldots,W(K)]$, where $W(t)$ is a multivariate vector of potential confounders measured at time $t$: socioeconomic and demographic variables, co-pollutants, and meteorologic variables.

Our modeling approach aims at the investigation of the effect of $A(t-1)$ on $Y(t)$. In this study, the outcome at time $t$ [$Y(t)$] and exposure at time $t-1$ [$A(t-1)$] are actually measured during the same quarter, which does not violate the time-ordering assumption on which are based valid causal inferences (the exposure precedes the outcome). Because we consider the effect of $O_3$ on asthma-related hospital discharges collected during quarters 2 and 3 only, we thus have 36 outcomes of interest rather than 72.

A typical assumption that is often not stated explicitly is that the observed data consist of $n$ independent and identically distributed observations from the random variable $O$ with distribution $P$. In this analysis, we make the assumption that the observed data consist of $n = 195$ random variables $O_i$ that describe each spatial/geographic unit $i$, $i = 1,\ldots,n$, each with distribution $P_i$. Under this assumption, it follows that mutual independence between the random variables $O_i$, conditional on the exposure regimen, is a reasonable approximation [see Supplemental Material for additional details (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)].

We chose to investigate the effect of $O_3$ on the asthma-related hospital discharge proportion for quarterly exposure to $O_3$ only; that is, we did not consider the effect of an $O_3$ history over multiple quarters. This decision was motivated by our view that most of the effect of $O_3$ could be captured by the exposure period of only one quarter—by estimation of the effect of $O_3$ during a given quarter on the outcome during that same quarter in the seasons with the highest levels of $O_3$. Because the experimental units are geographic areas rather than individuals, the population in the units was constantly changing over the 18-year study period; however, within a given quarter, the population was relatively stable. Another reason for selection of the short exposure period relates to power (sample size, $n = 195$) for identification of effects that extend over a longer exposure period (Neugebauer et al. 2007).

We estimated this effect of $O_3$ on the proportion of asthma-related hospital discharges with two approaches: the traditional method of regression of the proportion of asthma-related hospital discharges on $O_3$ and confounder; and a method based on history-restricted marginal structural models (HRMSMs) (Neugebaueret al. 2007). In contrast to the usual MSM approach, HRMSMs allow the investigator to specify the time interval over which the history of exposure is to be considered—a critical issue for this analysis.

For both approaches, working models considered were semiparametric linear models. The rationale for use of linear models is presented in the Supplemental Material (online at http://www.ehponline.org/members/2008/10497/suppl.pdf).

The deletion/substitution/addition (DSA) algorithm was used for all model selections required for the traditional approach and the nuisance parameters in the HRMSM approach (Sinisi and van der Laan 2004). This is a data-adaptive model selection procedure based on cross-validation that relies on deletion, substitution, and addition moves to search through a large space of possible polynomial models. The criterion for model selection is based not on $p$-values but on a loss function (empirical and cross-validated residual sum of squares). The DSA procedure is publicly available as an R package (http://www.stat.berkeley.edu/~laan/Software/). All 7,011 observations were provided to all DSA runs. The DSA assumes that data are missing at random when searching for the best predictive linear model of the proportion of asthma-related hospital discharges.

**Traditional regression approach.** The traditional approach to estimate the effect of $A(t-1)$ on $Y(t)$ is to regress the outcome, $Y(t)$, on the exposure, $A(t-1)$, and all confounders. Potential confounders are: $W\text{—}(t-1) = [W(1),\ldots,W(t-1)]$, $Y\text{–}(t-1)$, and $A\text{–}(t-1)$. Under the assumption of no unobserved confounders, this approach allows the investigation of the effects of $O_3$ at each quarter, $A(t-1)$, on $Y(t)$, conditional on the past confounders in the regression model. It is realistic to assume that $O_3$ levels before quarter $t$ [i.e., $A\text{–}(t-1)$] do not affect the outcome in quarter $t$; thus, we did not consider them as confounders. Similarly, we did not consider past quarter discharges [i.e., $Y\text{–}(t-1)$]. Among all potential covariates $W\text{—}(t-1)$, we only considered as potential confounders all same-quarter covariates $W(t-1)$ and only copollutants and meteorologic variables from the previous quarter and previous year included in $W(t-2)$ and $W(t-5)$. This allowed us to maximize control of possible long-term trends in other pollutants on the current quarter's outcome. Forty-seven remaining covariates were identified as potential confounders of the effect of $O_3$ at quarter $t-1$ on the proportion of asthma-related hospital discharges at quarter $t$. Among these 47 covariates, only 29 were considered in the analysis, based on their univariate association with the proportion of asthma-related hospital discharges and $O_3$ levels [see Supplemental Material, Table S1 (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)]; this subset of 29 potential confounders is denoted with $W\text{—} \times (t-1)$.

We selected a pooled model for $E[Y(t)|A(t-1), W\text{—} \times (t-1)]$ across time with the DSA [see Supplemental Material (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)]. The standard errors for the coefficients in the selected model were obtained with the generalized estimation equation procedure (semiparametric modeling with the independence correlation structure).

This traditional approach does not answer directly our original question of interest: the population-level effect of $A(t-1)$ on $Y(t)$; indeed, this method provides the estimate of the effect conditional on confounders $W\text{—} \times (t-1)$ which only correspond with the population-level effect estimate of interest when confounders are not effect modifiers.

**HRMSM.** To obtain an estimate of the population-level, causal effect of $O_3$ on the proportion of asthma-related hospital discharges, we applied an HRMSM (Neugebaueret al. 2007). HRMSMs have been developed to address situations where only part of the exposure history is relevant [for details, see Supplemental Material (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)]. The exposure period considered is a single quarter as opposed to the entire exposure history.

We implemented two estimators of HRMSM causal parameters: the inverse probability of treatment weighted (IPTW) and G-computation. Confidence intervals (CIs) and *p*-values for the two estimates were obtained with 10,000 bootstrap iterations, where resampling was based on the 195 independent grids.

## Results

Characteristics of the total population who resided in the study domain (Figure 1) over the 84 quarters (1980–2000) are summarized in Table 1. For a summary of the characteristics of the population of asthma discharges from birth to 19 years of age for quarters 2 and 3 for 1983–2000, see Supplemental Material, Table S4 (online at http://www.ehponline.org/members/2008/10497/suppl.pdf).

$O_3$ concentrations declined steadily over the entire study period [Supplemental Material, Figure S8_a (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)]. Median 1-hr maximum and 8-hr average median $O_3$ for quarters 2–3 declined across all grids (Figure 2). Median 1-hr maxima also declined in quarters 1 and 4 [Supplemental Material, Table S5 (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)]. Substantial declines were seen for the other pollutants as well [see Supplemental Material, Table S5, Figure S8_b (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)]. The distribution of the quarterly population was skewed toward areas at the lower two-thirds of the quarterly $O_3$ distributions [see Supplemental Material, Figure S9 (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)]. During 1980–2000, 25.7% of the gridded, quarterly, average 1-hr maximum $O_3$ concentrations exceeded the level of California's daily 1-hr standard (90 ppb), and 8.2% exceeded the federal daily 1-hr standard of 0.12 ppm. For quarters 2 and 3 and years 1983 through 2000, 47.5% and 13.2% of the quarterly, average, 1-hr maximum $O_3$ concentrations exceeded the California and federal daily 1-hr standard, respectively (California EPA 2008; U.S. EPA 2000).

The median 1-hr and 8-hr maximum average $O_3$ levels were highly correlated ($r = 0.99$) (Table 2). During 1980–2000, $O_3$ concentrations showed moderate correlation with $PM_{10}$ and little correlation with the other pollutants. $O_3$ and $PM_{10}$ are correlated on a quarterly averaging time, because wind-blown dust and resuspended road-dust emissions cause relatively high $PM_{10}$ levels during the dry season when $O_3$ levels also are high.

In the conventional regression model, the identical model was selected when $O_3$ was forced into the model or when the DSA was free to choose any variable (Table 3). Of the seven [of 29; see Supplemental Material, Table S1 (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)] other variables selected into the models, none was another pollutant (Table 3) [see Supplemental Material for details of model selection (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)]. Thus, it is unlikely that the association is confounded by other pollutants. In addition, time was not selected as a main effect or interaction variable—an observation indicating that the unit effect of $O_3$ on the proportion of asthma-related discharges was constant over the study period, despite the decline in the levels of $O_3$ and all other pollutants measured. The estimated effect of a 10-ppb increase in the quarterly average 1-hr maximum $O_3$ was 1.4 discharges per 105 age-eligible population (95% CI, 0.71–2.09 per 105 population). The final model was used to predict the proportion of discharges at the median O3 concentration (87.7 ppb) over all grids and all quarters (3.12× 10–4). A 10-ppb increase above this level is estimated to lead to a 4.6% increase in the proportion of discharges (3.26× 10–4).

To determine the extent to which time contributed to confounding, the DSA was run first only with time variables. When the time variables selected by the DSA were forced into a model that also forced in $O_3$ into the same model, no other variables were selected by the DSA. This indicates that the demographic variables included in the models in Table 3 were capturing the overall temporal confounding related to population demographic and other unmeasured time-varying factors. This is seen clearly in Figure 3.The model with only time variables shows a clear temporal trend in hospital discharges. In contrast, the model with $O_3$ and demographic variables shows a nearly constant proportion of hospital discharges over the study quarters.

To provide population-level estimates of pollutant effects, we used G-computation and IPTW to fit an HRMSM. Treatment models (models that relate cofounders to quarterly $O_3$ concentrations and include other confounding variables) on which IPTW estimation relies [Supplemental Material (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)] demonstrated that the experimental treatment assignment assumption was not tenable. We applied a diagnostic tool to assess the bias in the IPTW estimator due to the experimental treatment assignment (ETA) violation (Wang et al. 2006) and showed a 76% bias in comparison to the G-computation estimate (Table 4). Therefore, we relied on the G-computation estimator. The interpretation of the MSM parameter estimate is as follows: If, contrary to fact, the population experienced a 10-ppb increase in quarterly $O_3$, then hospital admissions would increase by $1.4 \times 10^5$ age-eligible population at any given quarter. This would represent the same effect estimated by the conventional regression analysis. In other words, the results from the MSM and conventional analyses, in this particular analysis, give identical parameter estimates because there are no interaction terms in the conventional model.

## Discussion

The most recent U.S. EPA synthesis of ambient $O_3$ health effects concludes that children with asthma suffer acute adverse health consequences at current ambient levels of $O_3$ (U.S. EPA 2006). Among these adverse outcomes, asthma-related hospital discharges are based on some of the least consistent data (see Figure 7-9, U.S. EPA 2006). In some studies, asthma discharges are not separated from other respiratory diseases of childhood (e.g., Burnett et al. 2001). Although some of the inconsistency likely relates to differences in populations and pollutant mixtures, some of it also could relate to the relatively short time periods (Atkinsonet al. 1999a, 1999b) and special circumstances (Friedmanet al. 2001) under which the data were collected and the inability to separate $O_3$ effects from those of other pollutants (Tolbertet al. 2000) The present ecologic study addresses these problems through evaluation of the relation between hospital discharges for asthma for infants, children, and adolescents and changes in warm-season ambient $O_3$ concentrations in a large, ethnically/racially diverse region of Southern California over 18 years (1983–2000). This region has seen changing

pollutant levels and population structure over both time and space during the study period. Of note is the decline in the percentage of native-born residents, from 40% in 1980 to 30% in 2000, and the decline in the percentage who listed their primary race/ethnicity as Caucasian, from approximately 80% in 1980 to approximately 60% in 2000 [see Supplemental Material for additional details (online at http://www.ehponline.org/members/2008/10497/suppl.pdf)].

Our data indicate that, despite consistent and substantial declines in ambient warm-season $O_3$ concentrations in the area of study (Figure 3A), there has been a time-independent, constant effect of ambient levels of $O_3$ on quarterly hospital discharge rates for asthma. For example, we estimate that the average effect of a 10-ppb mean increase in mean quarterly 1-hr maximum $O_3$ over the 18-year median of 87.7 ppb was a 4.6% increase (point estimate) in quarterly hospital discharges for asthma (increase from 3.12 to $3.26 \times 10^{-4}$ age-eligible population) over a time period in which the median age-eligible population was approximately 4 million persons. Moreover, from a regulatory policy perspective, if the national 8-hr maximum were set at 75 ppb instead of 70 ppb (~ 6.6 ppb difference in the 1-hr max), our results suggest that there could be an excess of $O_3$-season, asthma-related hospital admissions for children in the study area of approximately 3.0% (point estimate) above what could be expected at a more protective standard. Further, our data indicate that the $O_3$-related asthma discharges (the pollutant mixture remaining the same) would be affected by changes in demography that likely will occur; and caution needs to be exercised in terms of extrapolation into the future.

Several features of our analysis strengthen the quantitative estimates and the apparent lack of time dependence of the $O_3$ effect:

First, we used a very flexible, multiple cross-validation model fitting algorithm in which the constraints on the model were as follows: *a*) maximum model size of 10 variables; *b*) maximum power of any individual variable (includes time) of 3; and *c*) a maximum of two-way interactions between the 29 covariates considered, such that the sum of powers of each covariate in the interaction term is ≤ 3. Thus, the flexibility of the models allowed the description of complex associations between changing demography, meteorologic conditions, and all temporal confounders for which time was a surrogate. A direct by-product of this flexible model fitting is that the form of the $O_3$–hospital discharge relation was free to take any polynomial form over time. This approach is similar in flexibility to model fitting with spline functions.

Second, the 24-hr concentrations of $PM_{10}$, $NO_2$, and CO could enter the model at equivalent levels of complexity as $O_3$ and any other covariate and in interaction with time. Thus, we did not start with the *a priori* assumption that warm-season $O_3$ would be the only or the most important component of the four pollutants for which we warm-season data.

Third, we ran our analysis 10 separate times, each time with a different split for cross validation (equivalent to 50 splits of the data). All model runs selected $O_3$ and no other pollutant, and the identical model with covariates was selected 8 of 10 times (Table 3).

Fourth, we used an MSM approach to investigate the marginal (population-level) effects of $O_3$ on the outcome (Robins et al. 2000). This approach approximates what would have been observed if we could have randomized all of the spatial units at each time point to a quarterly mean $O_3$ concentration. The results of this analysis indicated that the conventional statistical association model, in this particular analysis, was equivalent to the G-computation estimates of the HRMSM parameters—an observation that is not surprising, given that there were no interactions in the association model. Therefore, under certain assumptions noted above, the $O_3$ parameter (Table 3) can be interpreted as a causal, unconditional (i.e., not stratum specific) population-level effect estimate. In other words, if, contrary to fact, the median quarterly average 1-hr maximum increased by 10 ppb in all geographic units, the quarterly average hospital discharge rate would be expected to increase by 1.4 discharges/$10^5$ age-eligible population. This causal interpretation relies on the counterfactual framework embodied in HRMSMs (Neugebaueret al. 2007), particularly the assumption of no unmeasured confounders. The fact that, in our analyses, the association between $O_3$ hospital discharges can be interpreted further as the population-level effect estimate of $O_3$ based on the G-computation estimator of an HRMSM relies on the critical assumption that the conventional associational model selected with the DSA algorithm is correctly specified (particularly the absence of interaction terms between $O_3$ and covariates), the assumption of correct model specification is embodied in all analyses of observational data. The inference for this causal effect estimate was obtained by bootstrap (without consideration of additional variability introduced by the model selection procedure as is the case with virtually all reports of conventional analyses). We are exploring alternate causal estimators of causal parameters that do not rely on the ETA assumption to validate the results presented in this paper to further verify the validity of the inference, and a preliminary assessment of this latter analysis is supportive. The full results of this alternative analysis are the subject of a subsequent paper.

Finally, the results demonstrate that the addition of $O_3$ and demographic variables to our analyses removed all of the time trend in the hospital discharge data (Figure 3). Finally, although we included discharges with a primary diagnosis of pneumonia or acute sinusitis, we do not think that this has biased our results. Our estimate of the median quarterly discharge rate for asthma is at the lower end of such estimates for all or part of the age range that we included (National Center for Health Statistics 2004).

It is difficult to compare our results with other studies because we used a different time reference—3-month intervals—in contrast to a daily time metric in most other studies (Burnettet al. 2001; Friedmanet al. 2001). The most important factor that governed the choice of the time metric related to the fact that, for practical purposes, $O_3$ is an outdoor pollutant whose indoor concentrations are determined by household ventilation (open windows, use of air conditioners) (Gonzales et al. 2003). Because people of all ages spend most of their days indoors (Wiley et al. 1991a, 1991b), we reasoned that a 3-month interval, based on typical patterns of $O_3$ concentrations to which people would be exposed during their times out of doors, would provide a more stable population-level estimate than would be the case for shorter time intervals, such as days or weeks. Several consequences stemmed from this choice. Because most studies of the health effects of short-term exposures to $O_3$ indicate that $O_3$ impacts on health occur within a few days after exposures (Galanet al. 2003; Mortimer et al. 2002), we did not feel that it was justified to lag population exposure by 3 months (i.e., one quarter). Therefore, we related $O_3$ concentration in a given quarter to hospital discharges in that quarter. On its face, this would appear to violate

the requirement for preservation of temporal sequence. However, given that we used average hospital discharges at the end of a quarter, this choice is valid. Furthermore, each of the 195 spatial units was assigned its spatially specific average quarterly discharge rate and $O_3$ concentration, and the data were treated as a repeated-measures problem over the 36 quarters; we have accounted for differences in the mean exposure over space and time. In this regard, some daily time-series studies may have violated the temporality assumption in that their designation of lag 0 often includes the day of hospital admission. To be sure that longer-term trends for other pollutants did not confound our $O_3$ exposure estimates, we considered previous quarter and previous year $PM_{10}$, $NO_2$, and CO.

The potential for spatial correlation to result in incorrect variance estimates for exposure outcome measures in time series studies of health effects of air pollutants has been noted (Ramsay et al. 2003a, 2003b). Although we did not perform a time-series analysis, we did address the issue of spatial correlation by not assuming that the data for each unit are obtained from independent draws from a common distribution but rather from each of 195 distributions whose similarity can be explained by close geographic proximity, conditional on the exposure regimen, and thus the independence assumption is reasonable.

Although we report the results as "$O_3$-related effects," $O_3$ is likely to be the best marker (of the pollutants available for analysis) for the gaseous oxidant species produced by the complex photochemistry that occurs in the SoCAB during the warm months of the year and involves oxides of nitrogen and hydrocarbons, largely from mobile source emissions. $O_3$ is the most abundant oxidant in the urban atmosphere; however, the mixture also includes peroxyacetylnitrate, hydrogen peroxide, organic peroxides, and the hydroxyl, hydroperoxy, and many organic peroxy radicals (Atkinson 1997). Several epidemiologic studies have shown that the oxidant properties of ambient air contribute to adverse health outcomes in persons with and without asthma (Grievink et al. 1998; Romieu et al. 1996, 1998, 2002). For example, Romieu et al. (2002) studied asthmatics in Mexico City and demonstrated that among the pollutant measurements for $SO_2$, $PM_{10}$, $NO_2$, and $O_3$, $O_3$ was most closely associated with decrements in lung function in children and were reversed by antioxidant vitamin supplementation. Relevant to our study, the effects were most marked in those with severe asthma—the pool of subjects out of which hospital admissions are most likely to occur. The findings in these studies have been supported by controlled $O_3$ exposure studies in which subjects were placed on diets supplemented with antioxidant vitamins and vegetable oils (Samet et al. 2001) and studies of airways reactivity after controlled $O_3$ exposure (Trenga et al. 2001).

In summary, we conducted exhaustive analyses to address many of the outstanding issues related to reported associations between $O_3$ and use of hospital services for asthma. Although additional work is ongoing to buttress the causal interpretation that we have given to our results, our data support and extend other observations that ambient $O_3$ (highly oxidant, ambient, warm-season environments) causes increases in hospital admissions in children with asthma. Moreover, the linearity of the relation that we observed indicates that these excess asthma hospital discharges can be expected to continue at levels of air quality experienced in southern California.

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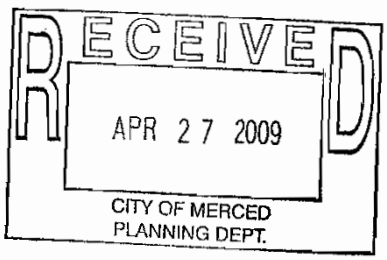

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# Ischemic and Thrombotic Effects of Dilute Diesel-Exhaust Inhalation in Men with Coronary Heart Disease

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## ABSTRACT

### BACKGROUND

Exposure to air pollution from traffic is associated with adverse cardiovascular events. The mechanisms for this association are unknown. We conducted a controlled exposure to dilute diesel exhaust in patients with stable coronary heart disease to determine the direct effect of air pollution on myocardial, vascular, and fibrinolytic function.

### METHODS

In a double-blind, randomized, crossover study, 20 men with prior myocardial infarction were exposed, in two separate sessions, to dilute diesel exhaust (300 $\mu$g per cubic meter) or filtered air for 1 hour during periods of rest and moderate exercise in a controlled-exposure facility. During the exposure, myocardial ischemia was quantified by ST-segment analysis using continuous 12-lead electrocardiography. Six hours after exposure, vasomotor and fibrinolytic function were assessed by means of intraarterial agonist infusions.

### RESULTS

During both exposure sessions, the heart rate increased with exercise ($P<0.001$); the increase was similar during exposure to diesel exhaust and exposure to filtered air ($P=0.67$). Exercise-induced ST-segment depression was present in all patients, but there was a greater increase in the ischemic burden during exposure to diesel exhaust (−22±4 vs. −8±6 millivolt seconds, $P<0.001$). Exposure to diesel exhaust did not aggravate preexisting vasomotor dysfunction, but it did reduce the acute release of endothelial tissue plasminogen activator ($P=0.009$; 35% decrease in the area under the curve).

### CONCLUSIONS

Brief exposure to dilute diesel exhaust promotes myocardial ischemia and inhibits endogenous fibrinolytic capacity in men with stable coronary heart disease. Our findings point to ischemic and thrombotic mechanisms that may explain in part the observation that exposure to combustion-derived air pollution is associated with adverse cardiovascular events. (ClinicalTrials.gov number, NCT00437138.)

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THE WORLD HEALTH ORGANIZATION (WHO) estimates that air pollution is responsible for 800,000 premature deaths worldwide each year.[1] Short-term exposure to air pollution has been associated with increases in cardiovascular morbidity and mortality, with deaths due to ischemia, arrhythmia, and heart failure.[2] In a large cohort study from the United States, Miller et al. recently reported that long-term exposure to air pollution increases the risk of death from cardiovascular disease by 76%.[3] These associations are strongest for fine particulate air pollutants (particulate matter of less than 2.5 $\mu$m in aerodynamic diameter [$PM_{2.5}$]), of which the combustion-derived nanoparticulate in diesel exhaust is an important component.[4] Substantial improvements in air quality have occurred in the developed world over the past 50 years, yet the association between $PM_{2.5}$ and mortality has no apparent threshold and is evident below current air-quality standards.[5]

Preclinical models of exposure to particulate air pollution demonstrate accelerated atherosclerotic plaque development[6] and increased in vitro[7] and in vivo[8] platelet aggregation. Epidemiologic and observational clinical studies suggest that exposure to air pollution may worsen symptoms of angina,[9] exacerbate exercise-induced myocardial ischemia,[10,11] and trigger acute myocardial infarction.[12,13] These clinical findings are limited by imprecision in the measurement of pollution exposure, the effect of potential confounding environmental and social factors, and the lack of mechanistic data.[14] Controlled exposures to air pollutants can help address these shortcomings by providing a precisely defined exposure in a regulated environment that facilitates investigation with validated biomarkers and surrogate measures of cardiovascular health. Using a carefully characterized exposure system, we have previously shown that exposure to dilute diesel exhaust in healthy volunteers causes lung inflammation,[15] depletion of airway antioxidant defenses,[16] and impairment of vascular and fibrinolytic function.[17]

To our knowledge, there have been no controlled exposures in patients with coronary heart disease, an important population that may be particularly susceptible to the adverse cardiovascular effects of air pollution. We assessed the effect of inhalation of dilute diesel exhaust on myocardial, vascular, and fibrinolytic function in a population of patients with stable coronary heart disease.

## METHODS

### SUBJECTS

Twenty men with stable coronary artery disease participated in this study, which was performed with the approval of the local research ethics committee, in accordance with the Declaration of Helsinki, and with the written informed consent of all participants.

All the men had proven coronary heart disease, with a previous myocardial infarction (>6 months before enrollment) treated by primary angioplasty and stenting, and were receiving standard secondary preventive therapy. Men with angina pectoris (Canadian Cardiovascular Society class ≥2), a history of arrhythmia, diabetes mellitus, uncontrolled hypertension, or renal or hepatic failure, as well as those with unstable coronary disease (acute coronary syndrome or symptoms of instability 3 months before enrollment), were excluded. All eligible volunteers were invited to a prestudy screening for exercise stress testing; subjects who were unable to achieve stage 2 of the Bruce protocol or who had marked changes on an electrocardiogram (left bundle-branch block, early ST-segment depression >2 mm) and those in whom hypotension developed were excluded. Current smokers and men with asthma, substantial occupational exposure to air pollution, or an intercurrent illness were also excluded from the study.

### STUDY DESIGN

Using a randomized, double-blind, crossover study design, we evaluated the subjects in two 8 a.m. sessions at least 2 weeks apart. In each session, the subjects were exposed to controlled amounts of dilute diesel exhaust or filtered air. Each subject was exposed for 1 hour in an exposure chamber, as previously described.[15] During each exposure, the subjects performed two 15-minute periods of exercise on a bicycle ergometer separated by two 15-minute periods of rest. For each subject, the ergometer workload was calibrated to achieve a ventilation of 15 liters per minute per square meter of body-surface area to ensure a similar exposure on both occasions. The workload was constant for both exposures and was equivalent to stage 2 of the Bruce protocol (range, 110 to 150 watts; 5 to 7 metabolic equivalents). All subjects were fitted with 12-lead Holter electrocardiographic monitors (Medical Lifecard 12 Digital Holter Recorder, Del Mar Reynolds). In accordance with

previous exposure studies in healthy volunteers, vascular assessments were made 6 to 8 hours after exposure to diesel exhaust or filtered air.[17]

### DIESEL-EXHAUST EXPOSURE

The diesel exhaust was generated from an idling Volvo diesel engine (Volvo TD45, 4.5 liters, 4 cylinders, 680 rpm) from low-sulfur gas-oil E10 (Preem), as described previously.[15] More than 90% of the exhaust was shunted away, and the remainder diluted with filtered air heated to 20°C (relative humidity approximately 50%) before being fed into a whole-body exposure chamber (3.0 m by 3.0 m by 2.4 m) at a steady-state concentration.

The chamber was monitored continuously for pollutants, with exposures standardized with the use of nitrogen oxide concentrations to deliver a particulate matter concentration of 300 $\mu$g per cubic meter (median particle diameter, 54 nm; range, 20 to 120). There was little variation between exposures in the mean (±SE) number of particles ($1.26\pm0.01\times10^6$ particles per cubic centimeter) or in the concentrations of nitrogen oxide (4.45±0.02 ppm), nitrogen dioxide (1.01±0.01 ppm), nitric oxide (3.45±0.03 ppm), carbon monoxide (2.9±0.1 ppm), and total hydrocarbon (2.8±0.1 ppm). The predominant polycyclic aromatic hydrocarbons (approximately 90% of the total) were phenanthrene, fluorene, 2-methylfluorene, dibenzothiophene, and different methyl-substituted phenanthrenes. Only a minor fraction of polycyclic aromatic hydrocarbons (3.5%) was associated with particulate matter: 0.04% total particulate matter and 0.06% particulate-matter organic fraction. The concentration of particulate matter of less than 10 $\mu$m in aerodynamic diameter ($PM_{10}$) in the exposure chamber exceeded the WHO air-quality standard of 50 $\mu$g per cubic meter by a factor of 6, and the nitrogen dioxide concentration exceeded the WHO standard of 0.105 ppm by a factor of 10.[18]

### VASCULAR STUDY

All subjects underwent brachial-artery cannulation with a 27-standard wire-gauge steel needle. After a 30-minute baseline saline infusion, subjects were given infusions of acetylcholine at rates of 5, 10, and 20 $\mu$g per minute (endothelium-dependent vasodilator, Clinalfa), bradykinin at rates of 100, 300, and 1000 pmol per minute (endothelium-dependent vasodilator that releases tissue plasminogen activator [t-PA], Clinalfa), and sodium nitroprusside at rates of 2, 4, and 8 $\mu$g per minute (endothelium-independent vasodilator, David Bull Laboratories); each infusion was given for 6 minutes. Infusions of the three vasodilators were separated by 20-minute saline infusions and given in a randomized order. Therapy with angiotensin-converting–enzyme inhibitors was withdrawn

**Table 1. Baseline Characteristics of the 20 Subjects with Coronary Heart Disease.***

| Characteristic | Value |
|---|---|
| Age (yr) | 60±1 |
| Smoking history (no. of subjects) | |
| Nonsmoker | 12 |
| Former smoker | 8 |
| Current smoker | 0 |
| Hypertension (no. of subjects) | 8 |
| Height (cm) | 173±6 |
| Weight (kg) | 79±3 |
| Body-mass index | 27±1 |
| Time since index infarction (mo) | 35±4 |
| Coronary angiographic findings | |
| No. of diseased vessels | |
| 1 | 13 |
| 2 | 6 |
| 3 | 1 |
| Culprit lesion (no. of subjects) | |
| Left anterior descending coronary artery | 14 |
| Circumflex coronary artery | 4 |
| Right coronary artery | 2 |
| Cholesterol (mg/dl) | |
| Total | 173±6 |
| LDL | 100±8 |
| HDL | 48±2 |
| Triglycerides (mg/dl) | 128±23 |
| Fasting glucose (mg/dl) | 102±6 |
| Medications (no. of subjects) | |
| Aspirin | 20 |
| Statin | 18 |
| Beta-blocker | 15 |
| ACE inhibitor or angiotensin-receptor blocker† | 4 |

* Plus–minus values are means ±SE. The body-mass index is the weight in kilograms divided by the square of the height in meters. LDL denotes low-density lipoprotein, HDL high-density lipoprotein, and ACE angiotensin-converting enzyme. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586. To convert the values for triglycerides to millimoles per liter, multiply by 0.01129. To convert the values for glucose to millimoles per liter, multiply by 0.05551.

† ACE inhibitor therapy was withdrawn 7 days before each vascular study. All other regular medications were continued throughout the study.

Table 2. Effect of Exercise on Heart Rate and ST Segment in the 20 Subjects during Exposures to Filtered Air and Diesel Exhaust.*

| Characteristic | Filtered Air | Diesel Exhaust | P Value† |
|---|---|---|---|
| **Exercise phase 1** | | | |
| Heart rate — bpm | | | |
| Baseline | 63±2 | 61±2 | 0.24 |
| Maximum | 87±3 | 86±3 | 0.67 |
| Maximum ST-segment change (μV) | | | |
| Lead II | −28±13 | −56±10 | 0.03 |
| Lead $V_2$ | −28±10 | −41±12 | 0.18 |
| Lead $V_5$ | −14±8 | −33±9 | 0.04 |
| Change in ischemic burden (mVsec) | | | |
| Lead II | −11±5 | −23±4 | 0.004 |
| Lead $V_2$ | −13±5 | −21±6 | 0.04 |
| Lead $V_5$ | −4±3 | −12±4 | 0.01 |
| **Exercise phase 2** | | | |
| Heart rate (bpm) | | | |
| Baseline | 67±2 | 65±2 | 0.35 |
| Maximum | 91±3 | 87±3 | 0.12 |
| Maximum ST-segment change (μV) | | | |
| Lead II | −17±15 | −49±12 | 0.006 |
| Lead $V_2$ | −18±12 | −41±13 | 0.04 |
| Lead $V_5$ | −7±9 | −28±10 | 0.02 |
| Change in ischemic burden (mVsec) | | | |
| Lead II | −8±6 | −22±4 | 0.0007 |
| Lead $V_2$ | −11±5 | −20±6 | 0.02 |
| Lead $V_5$ | −2±3 | −12±5 | 0.006 |

* Plus–minus values are means ±SE; mVsec denotes millivolt seconds.
† P values were calculated with Student's t-test.

7 days before each vascular study, because it augments bradykinin-induced release of endothelial t-PA.[19] All other medications were continued throughout the study.

Forearm blood flow was measured in both arms by venous occlusion plethysmography with the use of mercury-in-Silastic strain gauges, as described previously.[20] Heart rate and blood pressure in the noninfused arm were monitored at intervals throughout each study while the subject was in the supine position, with the use of a semiautomated, noninvasive oscillometric sphygmomanometer.

### FIBRINOLYTIC AND INFLAMMATORY MARKERS

Blood (10 ml) was withdrawn into acidified buffered citrate (Stabilyte tubes, Biopool International) for t-PA assays and into citrate (BD Vacutainer) for plasminogen activator inhibitor type 1 (PAI-1) assays. Plasma t-PA and PAI-1 antigen concentrations were determined by means of enzyme-linked immunosorbent assays (TintElize t-PA, Biopool EIA; Coaliza PAI-1; and Chromogenix AB). Serum C-reactive protein concentrations were measured with an immunonephelometric assay (BN II nephelometer, Dade Behring).

### DATA ANALYSIS

Electrocardiographic recordings were analyzed with the use of the Medical Pathfinder Digital 700 Series Analysis System (Del Mar Reynolds). ST-segment deviation was calculated by comparing the ST segment during each 15-minute exercise test with the average ST segment for the 15-minute period immediately before the start of the exposure. The ST-segment amplitude was determined at the J point plus 80 msec. The ischemic burden during each exercise test was calculated as the product of the change in ST-segment amplitude and the duration of exercise. Leads II, $V_2$, and $V_5$ were selected a priori for ST-segment analysis to reflect separate regions of myocardium. The maximum ST-segment depression and ischemic burden were determined for these leads individually and as a composite.

Plethysmographic data and net t-PA release were determined as described previously.[20,21]

### STATISTICAL ANALYSIS

Continuous variables are reported as means ±SE. Analysis of variance with repeated measures and a two-tailed Student's t-test were performed as appropriate with the use of GraphPad Prism software. A two-sided P value of less than 0.05 was considered to indicate statistical significance.

## RESULTS

Subjects were all middle-aged men with predominantly single-vessel coronary artery disease (Table 1). They reported no symptoms of angina and had no major arrhythmias during exposure or in the subsequent 24 hours.

### MYOCARDIAL ISCHEMIA

The heart rate increased with exercise during exposures to diesel exhaust and filtered air ($P<0.001$ for both comparisons with the baseline rates; $P=0.67$ for the comparison of rates during exposure to diesel exhaust and during exposure to filtered

air) (Table 2). Myocardial ischemia was detected during exercise in all subjects, with greater maximum ST-segment depression during exposure to diesel exhaust than during exposure to filtered air (Table 2 and Fig. 1A and 1B) ($P<0.05$). The ischemic burden induced by exercise was greater during exposure to diesel exhaust (Fig. 1C).

#### VASOMOTOR FUNCTION

There were no significant differences in resting heart rate, blood pressure, or baseline blood flow in the noninfused forearm between or during the two study visits. Although there was a dose-dependent increase in blood flow with each vasodilator ($P<0.001$ for all comparisons), neither endothelium-dependent nor endothelium-independent vasodilatation was affected by inhalation of diesel exhaust (Fig. 2). Comparison of these data with the findings in a contemporary reference population of healthy male volunteers (mean age, 53±4 years) showed impaired vasodilatation in response to acetylcholine ($P=0.02$) but not to sodium nitroprusside (Fig. 2).

#### FIBRINOLYTIC AND INFLAMMATORY MARKERS

There were no significant differences in basal plasma concentrations of t-PA (10.5±1.0 and 9.5±1.0 ng per milliliter, respectively) or its endogenous inhibitor, PAI-1 (18.8±3.0 and 17.0±2.0 ng per milliliter, respectively), 6 hours after exposure to either diesel exhaust or filtered air. Likewise, leukocyte, neutrophil, and platelet counts and serum C-reactive protein concentrations were not altered at 6 or 24 hours by exposure to diesel exhaust or filtered air. Bradykinin caused a dose-dependent increase in plasma t-PA concentrations (data not shown) and net t-PA release (Fig. 3) in the infused arm ($P<0.001$ for both comparisons) that was suppressed after exposure to diesel exhaust ($P=0.009$; 35% decrease in the area under the curve).

## DISCUSSION

We have demonstrated that transient exposure to dilute diesel exhaust, at concentrations occurring in urban road traffic, exacerbates exercise-induced myocardial ischemia and impairs endogenous fibrinolytic capacity in men with coronary heart disease. These findings provide a plausible explanation for the epidemiologic observation that exposure to air pollution is associated with adverse cardiovascular events.

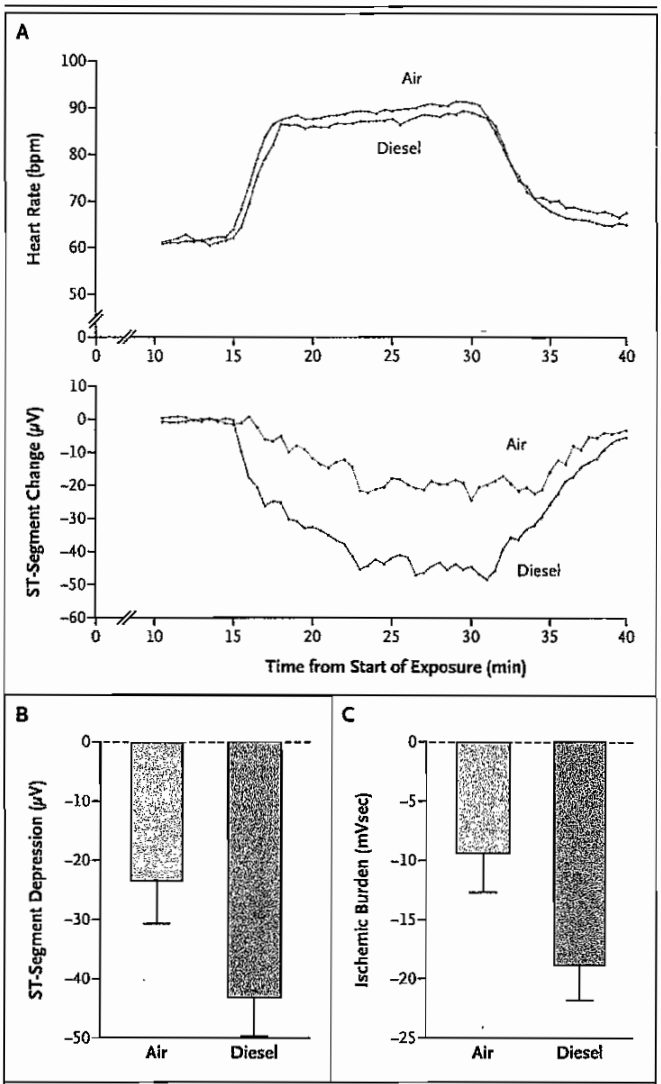


**Figure 1. Myocardial Ischemia during 15-Minute Intervals of Exercise-Induced Stress and Exposure to Diesel Exhaust or Filtered Air in the 20 Subjects.**

Panel A shows the average change in the heart rate and in the ST segment in lead II. Panel B shows the maximum ST-segment depression during inhalation of diesel exhaust as compared with filtered air ($P=0.003$), and Panel C shows the total ischemic burden during inhalation of diesel exhaust as compared with filtered air ($P<0.001$); the values in Panels B and C are averages of the values in leads II, $V_2$, and $V_5$. In all three panels, red indicates exposure to diesel exhaust, and blue exposure to filtered air. T bars denote standard errors, and mVsec millivolt seconds.

Concentrations of particulate matter can regularly reach levels of 300 μg per cubic meter in heavy traffic, in occupational settings, and in the world's largest cities.[22] A major proportion of this

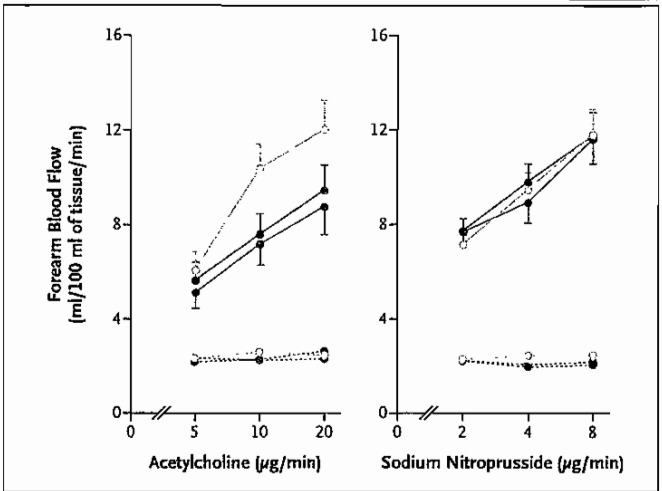


**Figure 2. Forearm Blood Flow 6 to 8 Hours after Exposures to Diesel Exhaust and Filtered Air.**

Values for infused (solid lines) and noninfused (dashed lines) forearm blood flow are shown for 17 subjects after exposure to diesel exhaust (red) and after exposure to filtered air (blue), as well as for a reference population of matched healthy controls (orange), during intrabrachial infusion of acetylcholine or sodium nitroprusside. P<0.001 for dose response to both drugs in the infused arm. Among the 17 subjects, P=0.54 for exposure to diesel exhaust versus filtered air during infusion of acetylcholine, and P=0.56 during infusion of sodium nitroprusside. For the comparison of the subjects with healthy controls, P=0.02 during acetylcholine infusion, and P=0.72 during sodium nitroprusside infusion.

mass is attributable to combustion-derived nanoparticles from traffic, ranging from 20% at remote monitoring sites[23] to 70% in a road tunnel.[24] Exposure to 300 μg of particulate matter per cubic meter for 1 hour increases a person's average exposure over a 24-hour period by only 12 μg per cubic meter. Changes of this magnitude occur on a daily basis, even in the least polluted cities, and are associated with increases in the rate of death from cardiorespiratory disorders.[25] Our model is therefore highly relevant, in terms of both the composition and the magnitude of exposure, to the assessment of short-term health effects in men.

Given potential safety concerns, we recruited patients who had stable and symptomatically well-controlled coronary heart disease, with good exercise tolerance on formal stress testing. The study participants were closely monitored throughout the exposure and reported no adverse effects. Despite similar changes in the heart rate during exposure to diesel exhaust and to filtered air, we documented asymptomatic myocardial ischemia that was increased by a factor of up to three after inhalation of diesel exhaust. This reproducible effect was present despite extensive use of maintenance beta-blocker therapy in patients without limiting angina. Thus, we have established that inhalation of diesel exhaust has an immediate, proischemic effect, and we believe this provides an important mechanism for the observed increase in myocardial infarction in the hour after exposure to traffic.[13]

Small areas of denudation and thrombus deposition are common findings on the surface of atheromatous plaques and are usually subclinical. Rosenberg and Aird have postulated that vascular-bed–specific defects in hemostasis exist and that propagation of coronary thrombosis is critically dependent on the local fibrinolytic balance.[26] The magnitude and rapidity of t-PA release from the vascular endothelium regulate the generation of plasmin and thus determine the efficacy of endogenous fibrinolysis.

We have previously reported impaired t-PA release in healthy volunteers 6 hours after inhalation of diesel exhaust, although this effect was not seen 2 hours after exposure.[17] We have now confirmed similar reductions in acute t-PA release 6 hours after inhalation of diesel exhaust in patients with coronary heart disease. This delayed effect on endogenous fibrinolysis cannot explain our findings of immediate myocardial ischemia but is consistent with the observations of Peters and colleagues, who reported a second peak in the incidence of myocardial infarction 5 to 6 hours after exposure to traffic.[13] Preclinical thrombotic models also lend support to our findings. Nemmar and colleagues reported that in a hamster model, instillation of diesel-exhaust particulate into the lungs increases venous and arterial thrombus formation at sites of vascular injury.[27] Taken together, these findings indicate an important thrombotic effect of diesel-exhaust inhalation that may promote coronary thrombosis.

Although we found important adverse effects of diesel exhaust on vascular fibrinolytic function, we did not detect an effect on vasomotor function. However, vasomotor function was assessed 6 hours after exposure and 5 hours after we documented an increase in the ischemic burden. We have previously demonstrated that exposure to diesel exhaust impairs vasomotor function in healthy volunteers.[17] This effect was most marked at 2 hours but was still present 6 hours after exposure. Therefore, we cannot exclude the possibil-

ity of a detrimental vasomotor effect in patients at an earlier point in time.

Patients with coronary heart disease are known to have impaired endothelial function,[28] and we confirm the presence of endothelial dysfunction in our patients. This may have hindered our ability to demonstrate a further impairment of vascular function after exposure to diesel exhaust. In addition, we performed our assessments while the subjects were taking medications that are known to influence endothelial vasomotor function.[29] Furthermore, Brook and colleagues reported that air pollution does not have an effect on endothelium-dependent vasodilatation.[30]

We have identified two distinct and potentially synergistic adverse cardiovascular effects of air pollution in patients with coronary heart disease. These effects may contribute to the increased incidence of myocardial infarction after exposure to traffic. However, the precise mechanisms by which diesel-exhaust inhalation induces these ischemic and thrombotic effects have not been established in our study and will need to be determined in future work.

Our findings are consistent with epidemiologic studies showing associations between ambient particulate air pollution and increased myocardial ischemia during formal exercise testing.[10,11] Myocardial ischemia occurs as a consequence of reduced myocardial oxygen supply, increased demand, or both. We hypothesize that oxidative stress and microvascular dysfunction in the resistance vessels of the myocardium may, in part, explain the adverse ischemic effects of exposure to dilute diesel exhaust. In vitro studies, animal models, and studies of exposures in humans have clearly established the oxidant and proinflammatory nature of combustion-derived particulate matter.[31] Indeed, the pattern of vascular dysfunction in our previous studies suggested that oxidative stress and reduced nitric oxide availability may play a role in mediating the adverse vascular effects of diesel-exhaust inhalation.[17]

Diesel exhaust is a complex mixture of gases and particles, and from our findings, we cannot rule out a nonparticulate cause of the adverse cardiovascular effects. However, on the basis of epidemiologic studies,[32] particulate matter is thought to be responsible for the majority of the adverse health effects of air pollution.[33] This view is supported by the recent observations of Miller and colleagues, who found that cardiovascular outcomes were strongly associated with long-term exposure to particulate matter but not with gaseous pollutants.[3] Ambient nitrogen dioxide can be considered a surrogate for pollution from traffic, but it has little adverse effect in controlled-chamber studies, even at the exposure levels in our study.[34] We therefore suggest that the cardiovascular effects described here are mediated primarily by the particulates in diesel exhaust and not by its other components. This argues for the use of diesel-exhaust particle traps to limit the adverse health effects of traffic emissions. However, the causative role of particulates must first be definitively established, and the efficacy of particle traps confirmed.

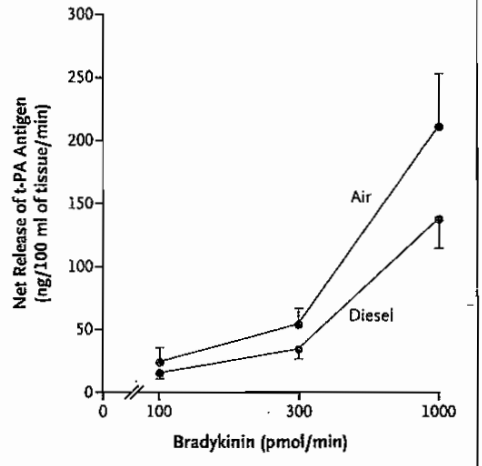


**Figure 3. Release of Tissue Plasminogen Activator (t-PA) Antigen 6 to 8 Hours after Exposures to Diesel Exhaust and Filtered Air in 17 Subjects.**

As compared with filtered air (blue), inhalation of diesel exhaust (red) reduced the net release of t-PA antigen (calculated as the product of forearm plasma flow and the difference in t-PA concentrations between the two arms) by 35% (P=0.009).

Brief exposure to dilute diesel exhaust increases myocardial ischemia and impairs endogenous fibrinolytic capacity in men with stable coronary heart disease. Our findings suggest mechanisms for the observation that exposure to combustion-derived air pollution is associated with adverse cardiovascular events, including acute myocardial infarction. Environmental health policy interventions targeting reductions in urban air pollution should be considered in order to decrease the risk of adverse cardiovascular events.

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No potential conflict of interest relevant to this article was reported.

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ORIGINAL ARTICLE

◂ Previous Volume 351:1057-1067 September 9, 2004 Number 11 Next ▸

# The Effect of Air Pollution on Lung Development from 10 to 18 Years of Age

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## ABSTRACT

*Background* Whether exposure to air pollution adversely affects the growth of lung function during the period of rapid lung development that occurs between the ages of 10 and 18 years is unknown.

*Methods* In this prospective study, we recruited 1759 children (average age, 10 years) from schools in 12 southern California communities and measured lung function annually for eight years. The rate of attrition was approximately 10 percent per year. The communities represented a wide range of ambient exposures to ozone, acid vapor, nitrogen dioxide, and particulate matter. Linear regression was used to examine the relationship of air pollution to the forced expiratory volume in one second ($FEV_1$) and other spirometric measures.

*Results* Over the eight-year period, deficits in the growth of $FEV_1$ were associated with exposure to nitrogen dioxide (P=0.005), acid vapor (P=0.004), particulate matter with an aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$) (P=0.04), and elemental carbon (P=0.007), even after adjustment for several potential confounders and effect modifiers. Associations were also observed for other spirometric measures. Exposure to pollutants was associated with clinically and statistically significant deficits in the $FEV_1$ attained at the age of 18 years. For example, the estimated proportion of 18-year-old subjects with a low $FEV_1$ (defined as a ratio of observed to expected $FEV_1$ of less than 80 percent) was 4.9 times as great at the highest level of exposure to $PM_{2.5}$ as at the lowest level of exposure (7.9 percent vs. 1.6 percent, P=0.002).

*Conclusions* The results of this study indicate that current levels of air pollution have chronic, adverse effects on lung development in children from the age of 10 to 18 years, leading to clinically significant deficits in attained $FEV_1$ as children reach adulthood.

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There is mounting evidence that air pollution has chronic, adverse effects on pulmonary development in children. Longitudinal studies conducted in Europe[1,2,3] and the United States[4,5,6] have demonstrated that exposure to air pollution is associated with reductions in the growth of lung function, strengthening earlier evidence[7,8,9,10,11,12] based on cross-sectional data. However, previous longitudinal studies have followed young children for relatively short periods (two to four years), leaving unresolved the question of whether the effects of air pollution persist from adolescence into adulthood. The Children's Health Study[13] enrolled children from 12 southern California communities representing a wide range of exposures to ambient air pollution. We documented the children's respiratory growth from the ages of 10 to 18 years. Over this eight-year period, children have substantial increases in lung function. By the age of 18 years, girls' lungs have nearly matured, and the growth in lung function in boys has slowed considerably, as compared with the rate in earlier adolescence.[14] We analyzed the association between long-term exposure to ambient air pollution and the growth in lung function over the eight-year period from the ages of 10 to 18 years. We also examined whether any observed effect of air pollution on this eight-year growth period results in clinically significant deficits in attained lung function at the age of 18 years.

## Methods

### Study Subjects

In 1993, the Children's Health Study recruited 1759 fourth-grade children (average age, 10 years) from elementary schools in 12 southern California communities as part of an investigation of the long-term effects of air pollution on children's respiratory health.[6,12,13] Data on pulmonary function were obtained by trained field technicians, who traveled to study schools annually from the spring of 1993 through the spring of 2001 to perform maximal-effort spirometric testing of the children. Details of the testing protocol have been published previously.[12] We analyzed three measures of pulmonary function: forced

vital capacity (FVC), forced expiratory volume in the first second ($FEV_1$), and maximal midexpiratory flow rate (MMEF). Pulmonary-function tests were not performed on any child who was absent from school on the day of testing, but such a child was still eligible for testing in subsequent years. Children who moved away from their recruitment community were classified as lost to follow-up and were not tested further. From the initial sample of the 1759 children in 1993, the number of children available for follow-up was 1414 in 1995, 1252 in 1997, 1031 in 1999, and 747 in 2001, reflecting the attrition of approximately 10 percent of subjects per year.

A baseline questionnaire, completed at study entry by each child's parents or legal guardian, was used to obtain information on the children's characteristics, including race, presence or absence of Hispanic ethnic background, level of parental education, presence or absence of a history of asthma diagnosed by a doctor, exposure to maternal smoking in utero, and household exposure to gas stoves, pets, and environmental tobacco smoke. Questions administered at the time of annual pulmonary-function testing were used to update information on asthma status, personal smoking status, and exposure to environmental tobacco smoke. The distribution of baseline characteristics of all study subjects and of two subgroups defined according to the length of follow-up (all eight years or less than eight years) is shown in the Supplementary Appendix (available with the full text of this article at www.nejm.org). The length of follow-up was significantly associated with factors related to the mobility of the population, including race, presence or absence of Hispanic ethnic background, presence or absence of exposure to environmental tobacco smoke, and parents' level of education. However, the length of follow-up was not significantly associated with baseline lung function or the level of exposure to air pollution, suggesting that the loss to follow-up did not differ with respect to the primary variables of interest.

The study protocol was approved by the institutional review board for human studies at the University of Southern California, and written informed consent was provided by a parent or legal guardian for all study subjects. We did not obtain assent from minor children, since this was not standard practice when the study was initiated.

**Air-Pollution Data**

Air-pollution–monitoring stations were established in each of the 12 study communities and provided continuous data, beginning in 1994. Each station measured average hourly levels of ozone, nitrogen dioxide, and particulate matter with an aerodynamic diameter of less than 10 μm ($PM_{10}$). Stations also collected two-week integrated-filter samples for measuring acid vapor and the mass and chemical makeup of particulate matter with an aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$). Acid vapor included both inorganic acids (nitric and hydrochloric) and organic acids (formic and acetic). For statistical analysis, we used total acid, computed as the sum of nitric, formic, and acetic acid levels. Hydrochloric acid was excluded from this sum, since levels were very low and close to the limit of detection. In addition to measuring $PM_{2.5}$, we determined the levels of elemental carbon and organic carbon, using method 5040 of the National Institute for Occupational Safety and Health.[15] We computed annual averages on the basis of average levels in a 24-hour period in the case of $PM_{10}$ and nitrogen dioxide, and a two-week period in the case of $PM_{2.5}$, elemental carbon, organic carbon, and acid vapor. For ozone, we computed the annual average of the levels obtained from 10 a.m. to 6 p.m. (the eight-hour daytime average) and of the one-hour maximal levels. We also calculated long-term mean pollutant levels (from 1994 through 2000) for use in the statistical analysis of the lung-function outcomes.

**Statistical Analysis**

The outcome data consisted of the results of 5454 pulmonary-function tests of 876 girls and 5300 tests of 883 boys over the eight-year period. We adopted a two-stage regression approach to relate the longitudinal pulmonary-function data for each child to the average air-pollution levels in each study community.

The first-stage model was a regression of each pulmonary-function measure (values were log-transformed) on age to obtain separate, community-specific average growth curves for girls and boys. To account for the growth pattern during this period, we used a linear spline model[14] that consisted of four straight lines over the age intervals of younger than 12 years, 12 to 14 years, 14 to 16 years, and older than 16 years, constrained to be connected at the three "knot" points. The model included adjustments for log values for height; body-mass index (the weight in kilograms divided by the square of the height in meters); the square of the body-mass index; race; the presence or absence of Hispanic ethnic background, doctor-diagnosed asthma, any tobacco smoking by the child in the preceding year, exposure to environmental tobacco smoke, and exercise or respiratory tract illness on the day of the test; and indicator variables for the field technician and the spirometer. In addition to these covariates, random effects were included to account for the multiple measurements contributed by each subject. An analysis of residual values confirmed that the assumptions of the model had been satisfied. The first-stage model was used to estimate the mean and variance of the growth in lung function over the eight-year period in each of the 12 communities, separately for girls and boys.

The second-stage model was a linear regression of the 24 sex- and community-specific estimates of the growth in lung function over the eight-year period on the corresponding average levels of each air pollutant in each community. Inverses of the first-stage variances were incorporated as weights, and a community-specific random effect was included to account for residual variation between communities. A sex-by-pollutant interaction was included in the model to evaluate whether there was a difference in the effect of a given pollutant between the sexes, and when this value was nonsignificant, the model was refitted to estimate the sex-averaged effect of the pollutant. Pollutant effects are reported as the difference in the growth in lung function over the eight-year period from the least to the most polluted community, with negative differences indicative of growth deficits with increasing exposure. We also considered two-pollutant models obtained by simultaneously regressing the growth in lung function over the eight-year period on pairs of pollutants.

In addition to examining the growth in lung function over the eight-year period, we analyzed the $FEV_1$ measurements obtained in 746 subjects during the last year of follow-up (average age, 17.9 years) to determine whether exposure to air pollution was associated with clinically significant deficits in attained $FEV_1$. We defined a low $FEV_1$ as an attained $FEV_1$ below 80 percent of the predicted value, a criterion commonly used in clinical settings to identify persons who are at increased risk for adverse respiratory conditions. To determine the predicted $FEV_1$, we first fitted a regression model for observed $FEV_1$ (using log-transformed values) with the following predictors: log-transformed height, body-mass index, the square of the body-mass index, sex, race or ethnic group,

asthma status, field technician, and interactions between sex and log-transformed height, sex and asthma, and sex and race or ethnic group. This model explained 71 percent of the variance in the attained $FEV_1$ level. For each subject, we then computed the predicted $FEV_1$ from the model and considered subjects to have a low $FEV_1$ if the ratio of observed to predicted $FEV_1$ was less than 80 percent. Linear regression was then used to examine the correlation between the community-specific proportion of subjects with a low $FEV_1$ and the average level of each pollutant from 1994 through 2000. This model included a community-specific random effect to account for residual variation. Regression procedures in SAS software[16] were used to fit all models. Associations denoted as statistically significant were those that yielded a P value of less than 0.05, assuming a two-sided alternative hypothesis.

## Results

From 1994 through 2000, there was substantial variation in the average levels of study pollutants across the 12 communities, with relatively little year-to-year variation in the annual levels within each community (Figure 1). From 1994 through 2000, the average levels of ozone were not significantly correlated across communities with any other study pollutant (Table 1). However, correlations between other pairs of pollutants were all significant, ranging from an R of 0.64 ($P<0.05$) for nitrogen dioxide and organic carbon, to an R of 0.97 ($P<0.001$) for $PM_{10}$ and organic carbon. Thus, nitrogen dioxide, acid vapor, and the particulate-matter pollutants can be regarded as a correlated "package" of pollutants with a similar pattern relative to each other across the 12 communities.

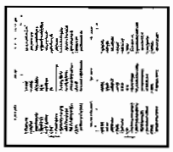

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**Figure 1.** Mean (+SD) Annual Average Levels of Pollutants from 1994 through 2000 in the 12 Study Communities in Southern California.

AL denotes Alpine, AT Atascadero, LE Lake Elsinore, LA Lake Arrowhead, LN Lancaster, LM Lompoc, LB Long Beach, ML Mira Loma, RV Riverside, SD San Dimas, SM Santa Maria, and UP Upland. $O_3$ denotes ozone, $NO_2$ nitrogen dioxide, and $PM_{10}$ and $PM_{2.5}$ particulate matter with an aerodynamic diameter of less than 10 μm and less than 2.5 μm, respectively.

**View this table:** **Table 1.** Correlation of Mean Air-Pollution Levels from 1994 through 2000 across the 12 Study Communities.
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Among the girls, the average $FEV_1$ increased from 1988 ml at the age of 10 years to 3332 ml at the age of 18 years, yielding an average growth in $FEV_1$ of 1344 ml over the eight-year period (Table 2). The corresponding averages in boys were 2082 ml and 4464 ml, yielding an average growth in $FEV_1$ of 2382 ml over the eight-year period. Similar patterns of growth over the eight-year period were observed for FVC and MMEF (Table 2).

**View this table:** **Table 2.** Mean Levels of Growth in Pulmonary Function during the Eight-Year Study Period, from 1993 to 2001.
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Although the average growth in $FEV_1$ was larger in boys than in girls, the correlations of growth with air pollution did not differ significantly between the sexes, as shown for nitrogen dioxide in Figure 2. The sex-averaged analysis, depicted by the regression line in Figure 2, demonstrated a significant negative correlation between the growth in $FEV_1$ over the eight-year period and the average nitrogen dioxide level ($P=0.005$). The estimated difference in the average growth in $FEV_1$ over the eight-year period from the community with the lowest nitrogen dioxide level to the community with the highest nitrogen dioxide level, represented by the slope of the plotted regression line in Figure 2, was −101.4 ml.

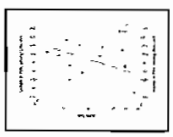

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**Figure 2.** Community-Specific Average Growth in $FEV_1$ among Girls and Boys During the Eight-Year Period from 1993 to 2001 Plotted against Average Nitrogen Dioxide ($NO_2$) Levels from 1994 through 2000.

Estimated differences in the growth of $FEV_1$, FVC, and MMEF during the eight-year period with respect to all pollutants are summarized in Table 3. Deficits in the growth of $FEV_1$ and FVC were observed for all pollutants, and deficits in the growth of MMEF were observed for all but ozone, with several combinations of outcome variables and pollutants attaining statistical significance. Specifically, for $FEV_1$ we observed significant negative correlations between the growth in this variable over the eight-year period and exposure to acid vapor ($P=0.004$), $PM_{2.5}$ ($P=0.04$), and elemental carbon ($P=0.007$), in addition to the above-mentioned correlation with nitrogen dioxide. As with $FEV_1$, the effects of the various pollutants on FVC and MMEF did not differ significantly between boys

and girls. Significant deficits in FVC were associated with exposure to nitrogen dioxide (P=0.05) and acid vapor (P=0.03), whereas deficits in MMEF were associated with exposure to nitrogen dioxide (P=0.02) and elemental carbon (P=0.04). There was no significant evidence that ozone, either the average value obtained from 10 a.m. to 6 p.m. or the one-hour maximal level, was associated with any measure of lung function. In two-pollutant models for any of the measures of pulmonary function, adjustment for ozone did not substantially alter the effect estimates or significance levels of any other pollutant (data not shown). In general, two-pollutant models for any pair of pollutants did not provide a significantly better fit to the data than the corresponding single-pollutant models; this was not surprising, given the strong correlation between most pollutants.

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**Table 3.** Difference in Average Growth in Lung Function over the Eight-Year Study Period from the Least to the Most Polluted Community.

The association between pollution and the growth in $FEV_1$ over the eight-year period remained significant in a variety of sensitivity analyses (Table 4). For example, estimates of the effect of acid vapor and elemental carbon (model 1 in Table 4) changed little with adjustment for in-utero exposure to maternal smoking (model 2), presence in the home of a gas stove (model 3) or pets (model 4), or parental level of education (model 5). To account for possible confounding by short-term effects of air pollution, we fitted a model that adjusted for the average ozone, nitrogen dioxide, and $PM_{10}$ levels on the three days before each child's pulmonary-function test. This adjustment also had little effect on the estimates of the long-term effects of air pollution (model 6). Table 4 also shows that the effects of pollutants remained large and significant in the subgroups of children with no history of asthma (model 7) and those with no history of smoking (model 8). The effects of pollutants were not significant among the 457 children who had a history of asthma or among the 483 children who had ever smoked (data not shown), although the sample sizes in these subgroups were small. Model 9 demonstrates that the extremes in pollutant levels did not drive the observed associations; in other words, we found similar effect estimates after eliminating the two communities with the highest and lowest levels of each pollutant. Finally, model 10 shows the effects of pollutants in the subgroup of subjects who underwent pulmonary-function testing in both 1993 and 2001 (i.e., subjects who participated in both the first and last year of the study). The magnitudes of effects in this subgroup were similar to those in the entire sample (model 1), suggesting that observed effects of pollutants in the entire sample cannot be attributed to biased losses to follow-up across communities. These sensitivity analyses were also applied to the other pollutants and to FVC and MMEF, with similar results.

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**Table 4.** Sensitivity Analysis of the Effects of Acid Vapor and Elemental Carbon on Growth in $FEV_1$ over the Eight-Year Study Period.

Pollution-related deficits in the average growth in lung function over the eight-year period resulted in clinically important deficits in attained lung function at the age of 18 years (Figure 3). Across the 12 communities, a clinically low $FEV_1$ was positively correlated with the level of exposure to nitrogen dioxide (P=0.005), acid vapor (P=0.01), $PM_{10}$ (P=0.02), $PM_{2.5}$ (P=0.002), and elemental carbon (P=0.006). For example, the estimated proportion of children with a low $FEV_1$ (represented by the regression line in Figure 3) was 1.6 percent at the lowest level of exposure to $PM_{2.5}$ and was 4.9 times as great (7.9 percent) at the highest level of exposure to $PM_{2.5}$ (P=0.002). Similar associations between these pollutants and a low $FEV_1$ were observed in the subgroup of children with no history of asthma and the subgroup with no history of smoking (data not shown). A low $FEV_1$ was not significantly correlated with exposure to ozone in any group.

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**Figure 3.** Community-Specific Proportion of 18-Year-Olds with a $FEV_1$ below 80 Percent of the Predicted Value Plotted against the Average Levels of Pollutants from 1994 through 2000.

The correlation coefficient (R) and P value are shown for each comparison. AL denotes Alpine, AT Atascadero, LE Lake Elsinore, LA Lake Arrowhead, LN Lancaster, LM Lompoc, LB Long Beach, ML Mira Loma, RV Riverside, SD San Dimas, SM Santa Maria, and UP Upland. $O_3$ denotes ozone, $NO_2$ nitrogen dioxide, and $PM_{10}$ and $PM_{2.5}$ particulate matter with an aerodynamic diameter of less than 10 μm and less than 2.5 μm, respectively.

## Discussion

The results of this study provide robust evidence that lung development, as measured by the growth in FVC, $FEV_1$, and MMEF from the ages of 10 to 18 years, is reduced in children exposed to higher levels of ambient air pollution. The strongest associations were observed between $FEV_1$ and a correlated set of pollutants, specifically nitrogen dioxide, acid vapor, and elemental carbon. The effects of these pollutants on $FEV_1$ were similar in boys and girls and remained significant among children with no history of asthma and among those with no history of smoking, suggesting that most children are susceptible to the chronic respiratory effects of breathing polluted air. The magnitude of the observed effects of air pollution on the growth in lung function during this age interval was similar to those that have been reported for exposure to maternal smoking[17,18] and smaller than those reported for the effects of personal smoking.[17,19]

Cumulative deficits in the growth in lung function during the eight-year study period resulted in a strong association between exposure to air pollution and a clinically low $FEV_1$ at the age of 18 years. In general, lung development is essentially complete in girls by the age of 18 years, whereas in boys it continues into their early 20s, but at a much reduced rate. It is therefore unlikely that clinically significant deficits in lung function at the age of 18 years will be reversed in

either girls or boys as they complete the transition into adulthood. Deficits in lung function during young adulthood may increase the risk of respiratory conditions — for example, episodic wheezing that occurs during a viral infection.[20] However, the greatest effect of pollution-related deficits may occur later in life, since reduced lung function is a strong risk factor for complications and death during adulthood.[21,22,23,24,25,26,27]

Deficits in lung function were associated with a correlated set of pollutants that included nitrogen dioxide, acid vapor, fine-particulate matter ($PM_{2.5}$), and elemental carbon. In southern California, the primary source of these pollutants is motor vehicles, either through direct tailpipe emissions or downwind physical and photochemical reactions of vehicular emissions. Both gasoline- and diesel-powered engines contribute to the tons of pollutants exhausted into southern California's air every day, with diesel vehicles responsible for disproportionate amounts of nitrogen dioxide, $PM_{2.5}$, and elemental carbon. In the current study, however, we could not discern the independent effects of pollutants because they came from common sources and there was a high degree of intercorrelation among them; similar difficulties have also been encountered in other studies of lung function and air-pollutant mixtures.[1,2,9,28,29,30] Since ozone is also formed during photochemical reactions involving fuel-combustion products, one might expect ozone to be correlated with the other study pollutants and therefore to show similar associations with lung function. However, the Children's Health Study was specifically designed to minimize the correlation of ozone with other pollutants across the 12 study communities. Thus, although ozone has been convincingly linked to acute health effects in many other studies,[11] our results provide little evidence that ambient ozone at current levels is associated with chronic deficits in the growth of lung function in children. Only a few other studies have addressed the long-term effects of ozone on lung development in children, and results have been inconsistent.[31] Although we found little evidence of an effect of ozone, this result needs to be interpreted with caution given the potential for substantial misclassification of exposure to ozone.[32,33]

The mechanism whereby exposure to pollutants could lead to reduced lung development is unknown, but there are many possibilities. Our observation of associations between air pollution and all three measures of lung function — FVC, $FEV_1$, and MMEF — suggests that more than one process is involved. FVC is largely a function of the number and size of alveoli, with differences in volume primarily attributable to differences in the number of alveoli, since their size is relatively constant.[34] However, since the postnatal increase in the number of alveoli is complete by the age of 10 years, pollution-related deficits in the growth of FVC and $FEV_1$ during adolescence may, in part, reflect a reduction in the growth of alveoli. Another plausible mechanism of the effect of air pollution on lung development is airway inflammation, such as occurs in bronchiolitis; such changes have been observed in the airways of smokers and of subjects who lived in polluted environments.[35,36]

A strength of our study was the long-term, prospective follow-up of a large cohort, with exposure and outcome data collected in a consistent manner throughout the study period. As in any epidemiologic study, however, the observed effects could be biased by underlying associations of the exposure and outcome to some confounding variables. We adjusted for known potential confounders, including personal characteristics and other sources of exposure to pollutants, but the possibility of confounding by other factors still exists. Over the eight-year follow-up period, approximately 10 percent of study subjects were lost to follow-up each year. Attrition is a potential source of bias in a cohort study if loss to follow-up is related to both exposure and outcome. However, we did not see evidence that the loss of subjects was related to either baseline lung function or exposure to air pollution. In addition, we observed significant associations between air pollution and lung growth in the subgroup of children who were followed for the full eight years of the study, with effects that were similar in magnitude to those in the group as a whole, thus making loss of subjects an unlikely source of bias.

We have shown that exposure to ambient air pollution is correlated with significant deficits in respiratory growth over an eight-year period, leading to clinically important deficits in lung function at the age of 18 years. The specific pollutants that were associated with these deficits included nitrogen dioxide, acid vapor, $PM_{2.5}$, and elemental carbon. These pollutants are products of primary fuel combustion, and since they are present at similar levels in many other areas,[37,38] we believe that our results can be generalized to children living outside southern California. Given the magnitude of the observed effects and the importance of lung function as a determinant of morbidity and mortality during adulthood, continued emphasis on the identification of strategies for reducing levels of urban air pollutants is warranted.

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## Source Information

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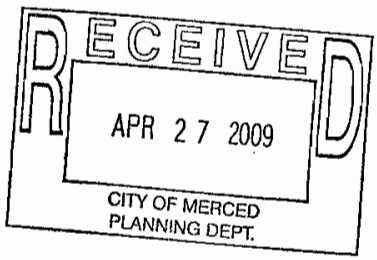

# Association between Air Pollution and Lung Function Growth in Southern California Children

## Results from a Second Cohort

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**A cohort of 1,678 Southern California children, enrolled as fourth graders in 1996, was followed for 4 years to determine whether the growth in lung function of the children was associated with their exposure to ambient air pollutants. These subjects comprised the second cohort of fourth grade children participating in the Children's Health Study. Significant deficits in lung function growth rate were associated with exposure to acid vapor, $NO_2$, particles with aerodynamic diameter less than 2.5 μm ($PM_{2.5}$), and elemental carbon. For example, the average annual growth rates of maximal midexpiratory flow and forced expiratory volume in 1 second were reduced by approximately 11% ($p = 0.005$) and 5% ($p = 0.03$), respectively, across the observed range of acid exposure. Exposure to acid vapor was also associated with reductions in the ratio of maximal midexpiratory flow to forced vital capacity ($p = 0.02$), whereas exposure to ozone was correlated with reduced growth in peak flow rate ($p = 0.006$). Larger deficits in lung function growth rate were observed in children who reported spending more time outdoors. These findings provide important replication of our previous findings of an effect of air pollution on lung function growth that were based on the first fourth-grade cohort from the Children's Health Study (*Am J Respir Crit Care Med* 2000;162:1383–1390).**

**Keywords:** lung function growth; children; air pollution

In a recent report, we described an association in children between long-term exposure to outdoor air pollutants and reductions in the growth of lung function (1). The data were obtained from the Children's Health Study (CHS), a 10-year investigation of children's respiratory health in 12 Southern California communities. On the basis of data on 1,498 children who entered the CHS as fourth graders in 1993 and who were followed for 4 years until 1997 (Cohort 1), we found a nearly 10% reduction in the growth rate per year of $FEV_1$ and maximal midexpiratory flow (MMEF) in the most polluted communities compared with that in the least polluted communities. The pollutants linked to these reductions were particles with aerodynamic diameter less than 10 μm ($PM_{10}$), $PM_{2.5}$, $NO_2$, and inorganic acid vapor. We were unable to disentangle the independent effects of these pollutants due to their high degree of correlation across communities. No significant associations were observed between lung function growth and ozone. Two other studies, one conducted in Austria (2) and the other in Poland (3), have also reported associations between ambient air pollutants and lung function growth in children. Collectively, these studies strengthen earlier evidence (4–7) that long-term exposure to air pollution can produce chronic health effects.

The design of the CHS has provided us the opportunity to attempt replication of our earlier findings. In 1996, we enrolled a second cohort of 2,081 fourth grade children (Cohort 2) from the same 12 study communities. Data collection protocols were the same as those used for Cohort 1. This report focuses on the relationship between air pollution and lung function development of the children in Cohort 2 over the 4-year period from 1996 to 2000. Side-by-side comparisons of pollutant-effect estimates from Cohorts 1 and 2 will also be provided.

## METHODS

### Study Subjects

Details of the CHS community selection, subject recruitment, and study design have been published previously (7, 8). Cohort 2 consisted of 2,081 fourth grade children (average age, 9.9 years) enrolled in 1996 from 12 Southern California communities. Baseline information for each child, including medical history and housing characteristics, was obtained via questionnaires filled out by a parent or guardian. In the spring of 1996, and every spring thereafter, a team of CHS field technicians traveled to study schools to measure participants' lung function. A rolling-seal spirometer (Spiroflow; P.K. Morgan Ltd., Gillingham, UK) was used to obtain up to seven maximal forced expiratory maneuvers on each child. A more detailed description of the pulmonary function testing protocol has been reported previously (7). A total of 1,678 children had at least two pulmonary function tests (PFT) from 1996 to 2000 and had complete data on all adjustment variables (described below). Outcome measures analyzed in this report include FVC, $FEV_1$, MMEF (also known as $FEF_{25-75\%}$), the ratio MMEF/FVC, and peak expiratory flow rate (PEFR). The study protocol was approved by the institutional review board for human studies at the University of Southern California, and consent was provided by parents for all study subjects.

### Air Pollution Data

Air pollution monitoring stations were in place in each of the 12 study communities for the duration of subject follow-up, and pollution levels were monitored continuously throughout each study year. Stations measured hourly concentrations of ozone ($O_3$), $PM_{10}$, and $NO_2$ and obtained filter-based 2-week integrated samples for measuring $PM_{2.5}$ and acid vapor. The latter included both inorganic (nitric, hydrochloric) and organic (formic, acetic) acids. For statistical analysis, we created an acid vapor metric as the sum of nitric, formic, and acetic acid concentrations. Hydrochloric acid was excluded from this sum because the concentrations over a 2-week period were very low and close to the detection limit. In addition to measuring $PM_{2.5}$ mass, we determined concentrations of elemental carbon (EC) and organic carbon (OC) using the NIOSH 5040 method (9). The $PM_{2.5}$ filter was also analyzed for concentrations of nitrate, sulfate, and ammonium, but

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these levels were so highly correlated with $PM_{2.5}$ mass across communities that we chose not to include them in this report. We computed the annual average of the 24-hour ($O_3$, $PM_{10}$, $NO_2$) or 2-week ($PM_{2.5}$, EC, OC, acid) average concentrations. For $O_3$, we also computed the annual average of the 10:00 A.M. to 6:00 P.M. average. Analogous hour-specific averages for $PM_{10}$ and $NO_2$ were not used, as they were highly correlated with their corresponding 24-hour averages. We computed the mean over 4 years (1996–1999) of the annual average concentrations in each community and used these in the statistical analysis of lung function growth.

### Statistical Analysis

To investigate the relationship between lung function growth and air pollution, we applied the same analytic approach as that previously applied to Cohort 1 (1). The data consisted of 7,106 PFT obtained over the 4-year period on 1,678 study subjects. We used a 3-level regression modeling approach to investigate variation in lung function growth across the 12 communities in relation to variation in average air quality, with adjustment for individual and time-varying covariates. Details of each regression model are given below.

The first model was a linear regression of 7,106 log-transformed lung function measures on age, to estimate each subject's intercept and growth slope. This model included adjustment for time-varying covariates, including height, body mass index, subject report of doctor-diagnosed asthma and cigarette smoking in the previous year, report of respiratory illness and exercise on the day of the test, and interactions of each of these variables with sex to allow for male–female differences. The models also included barometric pressure, temperature at test time, and sets of indicator variables for field technician and spirometer.

The second model was a linear regression of the 1,678 person-specific adjusted growth slopes from the first model on a set of community indicators, to obtain the mean growth slope for children in each of the 12 communities. Adjustments were made for person-specific covariates, including sex, race/ethnicity, and baseline report of asthma. Residuals from both the first and second linear regression models satisfied the model assumptions of normality and homoscedasticity.

The final model was a linear regression of the 12 community-average lung function growth rates on 4-year community-average pollution level. The parameter of interest was the slope from this third regression, which was reported as the difference in estimated percent growth rate per year between the most and the least polluted communities. Negative pollutant-effect estimates indicate reduced lung function growth with increased exposure. The pollutant-specific range from the least to the most polluted community was used for scaling to facilitate comparison of effect estimates among different pollutants. Each pollutant was analyzed separately for its relationship to lung function growth, and scatterplots were used to display the relationships graphically. We also estimated the effect of each pollutant after adjustment for each of the other pollutants, by regressing the community-average growth rates on pairs of pollutants.

A single mixed model that combined all three of the aforementioned regression models was used to estimate pollutant effects and to test hypotheses. The MIXED procedure in SAS (10) was used to fit the models. A two-sided alternative hypothesis and a 0.05 significance level were assumed in all testing. The primary analyses used all study subjects. However, we also conducted separate analyses in strata defined by time spent outdoors, as this factor was believed *a priori* to be important in determining a given child's exposure to the ambient pollutants under study. Children were asked how much time they spent outdoors between 3:00 P.M. and 6:00 P.M. on each of five weekday afternoons. We classified each child as "more outdoors" or "less outdoors" on the basis of whether the average time spent outdoors over the 5-day period was above or below the median time for all children. We also considered sex, baseline asthma status, and race/ethnicity as possible pollutant-effect modifiers, and we added appropriate interaction terms to the mixed model to test these hypotheses.

In addition to our analysis of Cohort 2, we show pollutant-effect estimates for Cohort 1 for comparison. The lung function and air pollutant data used for Cohort 1 were based on the first 4 years of follow-up of that cohort (1993–1997), as described in our previous report (1). However, that report did not include analysis of EC, as data on EC concentrations have only recently become available. To facilitate direct comparison across cohorts, we scaled pollutant effects for Cohort 1 to the same range as that used for Cohort 2 (i.e., to the difference from the least to the most polluted community over the Cohort 2 study period).

## RESULTS

Annual average pollutant levels for each community during the Cohort 2 study period are shown in Figure E1 (*see* online data supplement). Compared with the variation between communities, there was relatively little variation within communities over the 4-year observation period. Table 1 shows pairwise correlations between community average air pollution levels over the study period. Ozone concentrations (both 24-hour and 10 A.M.–6 P.M. average) were not significantly correlated with any other pollutant, with the exception of a negative correlation between 24-hour ozone and $NO_2$ ($r = -0.60$). However, the remaining pollutants were correlated with one another, with coefficients ranging from $r = 0.58$ (OC with $NO_2$) to $r = 0.97$ (OC with $PM_{10}$).

The Cohort 2 sample consisted of roughly equal numbers of males and females and included 52% white non-Hispanics, 32% Hispanics, and approximately 5% each of black, Asian, and other ethnic groups (Table 2). Overall, 14% of subjects reported doctor diagnosis of asthma at baseline, ranging from 8% (Riverside) to 19% (San Dimas). Between the weekday hours of 3:00 P.M. and 6:00 P.M., children spent an average of 1.3 hours outdoors, with most children spending between 0.5 and 2.3 hours outdoors during this time. An average of 4.3 PFT (of a possible 5) was recorded on each study subject.

**TABLE 1. CORRELATIONS AMONG COMMUNITY MEAN POLLUTION LEVELS**

| Pollutant† | $O_3$ | $NO_2$ | Acid Vapor | $PM_{10}$ | $PM_{2.5}$ | $PM_{10}$–$PM_{2.5}$ | Elemental Carbon | Organic Carbon |
|---|---|---|---|---|---|---|---|---|
| $O_3$, 10 A.M.–6 P.M. | 0.77** | −0.23 | 0.30 | 0.13 | 0.14 | 0.10 | −0.05 | 0.11 |
| $O_3$ | | −0.60* | −0.22 | −0.37 | −0.39 | −0.31 | −0.48 | −0.34 |
| $NO_2$ | | | 0.83*** | 0.64* | 0.77** | 0.46 | 0.93*** | 0.58* |
| Acid vapor‡ | | | | 0.79** | 0.87*** | 0.63* | 0.90*** | 0.74* |
| $PM_{10}$ | | | | | 0.95*** | 0.95*** | 0.86*** | 0.97*** |
| $PM_{2.5}$ | | | | | | 0.81** | 0.93*** | 0.89*** |
| $PM_{10}$–$PM_{2.5}$ | | | | | | | 0.71* | 0.96*** |
| Elemental carbon | | | | | | | | 0.81** |

*Definition of abbreviation*: $PM_{10}$ = particles with aerodynamic diameter less than 10 μm.
* $p < 0.05$.
** $p < 0.005$.
*** $p < 0.0005$.
† 24-hour average (unless otherwise noted) pollution level from 1996 to 1999.
‡ Acid vapor is the sum of nitric, formic, and acetic acid vapor concentrations.

TABLE 2. CHARACTERISTICS OF THE STUDY POPULATION

| | No. of Subjects* | Mean No. of PFTs | Female Sex (%) | Race Distribution, % | | | | | Ever Asthma† (%) | No. of Hours Outdoors‡ | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | White | Hispanic | Asian | Black | Other | | Median | 10th, 90th |
| Alpine | 157 | 4.2 | 50 | 76 | 19 | 1 | 0 | 3 | 14 | 1.7 | (0.8, 2.6) |
| Alascadero | 144 | 4.3 | 44 | 74 | 17 | 1 | 1 | 8 | 18 | 1.4 | (0.7, 2.4) |
| Lake Elsinore | 139 | 4.2 | 53 | 55 | 32 | 4 | 1 | 6 | 13 | 1.4 | (0.6, 2.4) |
| Lake Arrowhead | 145 | 4.3 | 52 | 71 | 22 | 0 | 1 | 6 | 14 | 1.1 | (0.4, 1.8) |
| Lancaster | 159 | 3.8 | 52 | 51 | 30 | 3 | 10 | 6 | 16 | 1.4 | (0.6, 2.3) |
| Lompoc | 147 | 4.3 | 47 | 46 | 37 | 9 | 5 | 3 | 10 | 1.1 | (0.3, 2.1) |
| Long Beach | 133 | 4.2 | 44 | 33 | 22 | 14 | 23 | 8 | 15 | 1.2 | (0.5, 2.3) |
| Mira Loma | 125 | 4.3 | 51 | 40 | 54 | 2 | 1 | 2 | 15 | 1.2 | (0.6, 2.1) |
| Riverside | 126 | 4.3 | 55 | 41 | 39 | 1 | 11 | 8 | 8 | 1.4 | (0.6, 2.6) |
| San Dimas | 141 | 4.5 | 52 | 48 | 36 | 10 | 1 | 5 | 19 | 1.1 | (0.3, 2.3) |
| Santa Maria | 133 | 4.0 | 51 | 20 | 62 | 9 | 2 | 7 | 13 | 1.1 | (0.5, 2.4) |
| Upland | 129 | 4.4 | 50 | 66 | 18 | 9 | 5 | 3 | 12 | 1.2 | (0.3, 2.0) |
| All | 1,678 | 4.3 | 50 | 52 | 32 | 5 | 5 | 6 | 14 | 1.3 | (0.5, 2.3) |

*Definition of abbreviation*: PFT = pulmonary function test.
* Number of subjects with at least two PFTs from 1996 to 2000.
† Doctor-diagnosed asthma at baseline.
‡ Number of hours spent outdoors on weekdays between 3:00 P.M. and 6:00 P.M.; values are the median and the 10th and 90th percentiles.

Over the 4-year study period, $FEV_1$ increased at an average rate of 11.8% per year in the cohort, with equivalent growth rates in males and females. However, the average $FEV_1$ growth rates varied across the 12 communities, from 11.0 to 12.4%. Figure 1 shows a plot of the community-specific growth rates versus the corresponding 4-year average pollutant concentrations. There was a significant negative correlation between $FEV_1$ growth rates and acid vapor ($r = -0.55$, $p = 0.03$). The predicted growth rates, depicted by the plotted regression line, decreased from 12.1 to 11.5% across the range of observed acid concentrations. This absolute difference of 0.6% corresponds to a relative reduction of 5% in average $FEV_1$ growth rate for those exposed to the highest compared with those exposed to the lowest observed acid concentration (i.e., 0.6%/12.1%). Negative correlations were also observed between $FEV_1$ growth rates and the other pollutants, but none achieved statistical significance. Analogous plots are shown for MMEF growth in Figure 2. MMEF growth rates were negatively correlated with concentrations of acid vapor ($p = 0.005$), $NO_2$ ($p = 0.02$), $PM_{2.5}$ ($p = 0.05$), and EC ($p = 0.04$). The predicted MMEF growth rates declined from approximately 11.6 to 10.3% across the range of observed acid concentrations, with this absolute difference of 1.3% corresponding to a relative reduction of 11%.

Table 3 shows the estimated absolute differences in growth rates from the most to the least polluted community for the five PFT measures and for all pollutants. Although most pollutant-effect estimates were negative for FVC, none achieve statistical significance. The associations of $FEV_1$ and MMEF with acid vapor shown in Figures 1 and 2, respectively, also held for nitric and formic acids separately and to a smaller extent for acetic acid. The ratio MMEF/FVC was correlated with $NO_2$ ($p = 0.04$), acid vapor ($p = 0.02$), and nitric ($p = 0.01$) and formic acids ($p = 0.02$). Each pollutant-effect estimate for MMEF/FVC (e.g., −0.96% for acid vapor) was approximately equal to the difference between the corresponding pollutant-effect estimates for MMEF (e.g., −1.28%) and FVC (e.g., −0.33%). The predicted PEFR growth declined by 1.2% across the range of 10 A.M.–6 P.M. $O_3$ ($p = 0.006$). None of the PFT measures was significantly associated with 24-hour $O_3$, $PM_{10}$, $PM_{10}$–$PM_{2.5}$, or OC. Adjustment for indoor sources of air pollution, including a gas stove, any pet, a cat, a dog, or a tobacco-smoking parent in the home, did not alter any pollutant-effect estimate by more than 10% of its unadjusted values (data not shown). We therefore concluded that any differences among communities in the prevalence of these indoor sources of air pollution did not confound the ambient pollutant-effect estimates. Additionally, there was no significant evidence of pollutant-effect modification by sex, ethnicity, or asthma status. As an example of the similarity in pollutant-effect estimates by asthma status, the decline in $FEV_1$ growth rate across the observed range of acid vapor was 0.50% in individuals with asthma and 0.63% in individuals without asthma, a difference that was not statistically significant ($p = 0.75$).

In two-pollutant models for $FEV_1$, effect estimates for acid vapor remained negative after adjustment for any other pollutant (Table 4, third row). On the other hand, adjustment for acid (Table 4, third column) substantially changed the univariate estimates (Table 4, main diagonal) of all other pollutants except for $O_3$. Table 5 shows similar two-pollutant analysis of MMEF. Here again, estimates of the acid vapor–effect remained negative with adjustment for any other pollutant, whereas adjustment for acid altered the effect estimate of every other pollutant. For example, the estimated univariate $NO_2$ effect (−1.10%) dropped in magnitude (0.03%) and became nonsignificant with adjustment for acid. For both $FEV_1$ and MMEF, the only two-pollutant model in which both pollutants were statistically significant predictors of growth included 10 A.M.–6 P.M. $O_3$ and $NO_2$, indicating that these pollutants might each contribute independently to reduced lung function growth. For example, the estimated effects on MMEF from this two-pollutant model were −1.11% ($p = 0.02$) for $O_3$ (Table 5, row 1, column 2) and −1.31% ($p = 0.003$) for $NO_2$ (Table 5, row 2, column 1). In additional models, inclusion of an $O_3$-by-$NO_2$ interaction did not significantly improve model fit for either $FEV_1$ or MMEF.

The directions and magnitudes of pollutant effects observed in Cohort 2 were generally comparable to those observed in Cohort 1 (Table 6). As an example, for $FEV_1$, the acid-effect estimates in Cohorts 1 and 2 were −0.82% ($p = 0.01$) and −0.63% ($p = 0.03$), respectively, and the corresponding acid-effect estimates for MMEF were −1.16% ($p = 0.02$) and −1.28% ($p = 0.005$), respectively. For all combinations of PFT and pollutant shown in Table 6, we formally tested whether the pollutant-effect estimates were different between the two cohorts; no significant differences were detected.

In each cohort, the strength of the pollutant effects was greater in children who reported spending more time out-

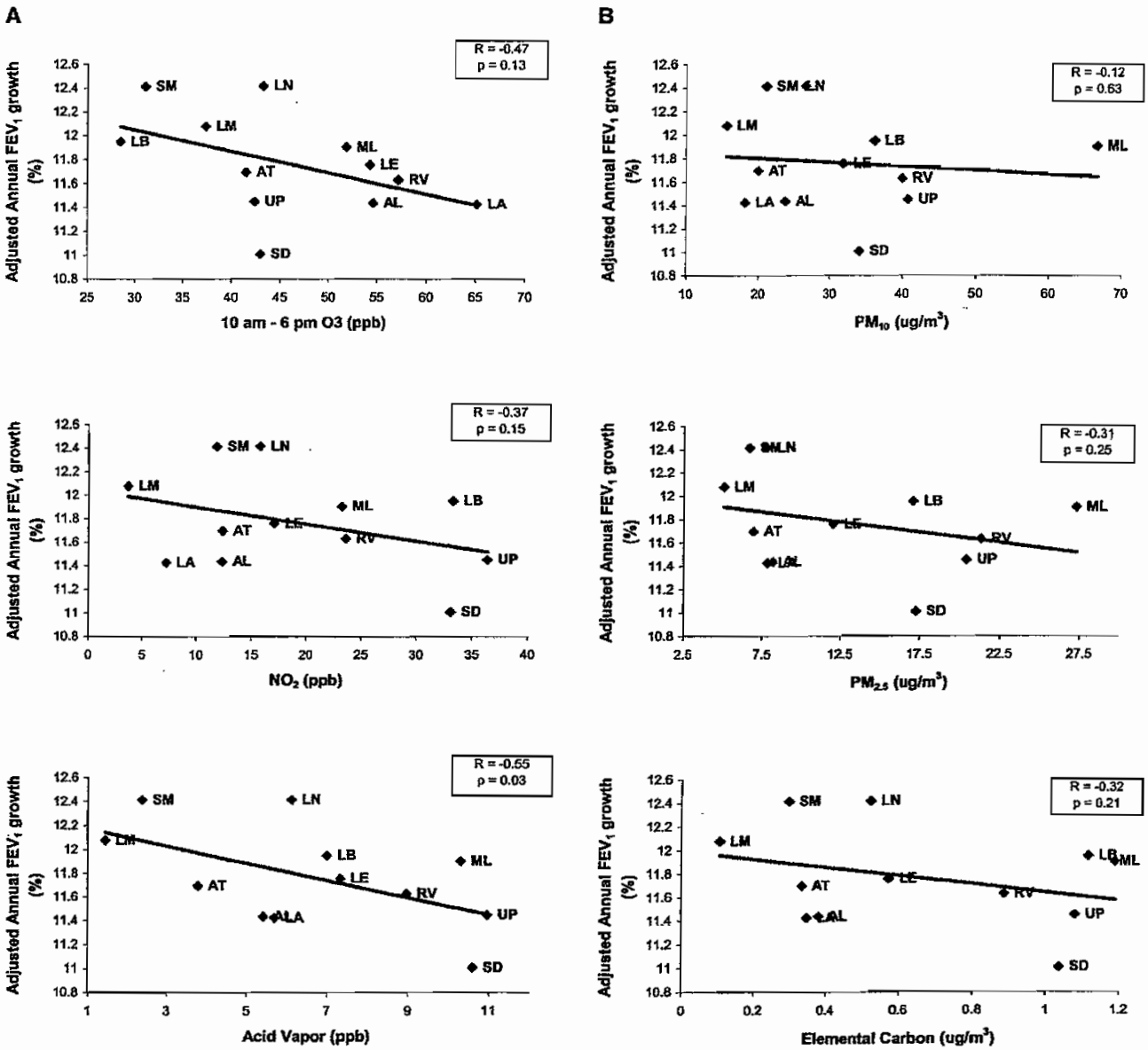


*Figure 1.* Adjusted average annual $FEV_1$ growth rates in the 12 communities versus the mean pollutant concentrations over the study period. AL = Alpine; AT = Atascadero; LE = Lake Elsinore; LA = Lake Arrowhead; LN = Lancaster; LM = Lompoc; LB = Long Beach; ML = Mira Loma; RV = Riverside; SD = San Dimas; SM = Santa Maria; UP = Upland.

doors (Table 7). For example, across the range of acid vapor, $FEV_1$ growth rates in the more-outdoors children declined by 1.1% in Cohort 1 ($p = 0.02$) and by 1.0% in Cohort 2 ($p = 0.002$). The corresponding declines in growth rate in the less-outdoors children were only 0.4% in Cohort 1 ($p = 0.18$) and 0.3% in Cohort 2 ($p = 0.45$). Several other statistically significant associations between PFT growth and pollutants were observed in the more-outdoors children, whereas no significant associations were observed in the more-indoors children.

## DISCUSSION

The results, based on the second fourth-grade cohort from the CHS, provide further evidence that ambient levels of air pollution in southern California have a detrimental effect on lung function growth in children. These findings are in general agreement with the results that were based on the first fourth-grade cohort (1). Also replicated from the Cohort 1 analysis is the finding of larger pollutant effects in children who reported spending more time outdoors. The replication of a previous result and the observation of a larger health effect in those who were more exposed are results that support a causal association. Additional studies in other populations are needed to further assess causal relationships.

Across cohorts and lung function measures, we observed significant associations with several of the pollutants, including both particles and gases. Although the correlations among pollutants were generally high, some trends emerged from the analysis of the two cohorts. For example, fine particles ($PM_{2.5}$) and the EC portion of $PM_{2.5}$ generally showed stronger associations

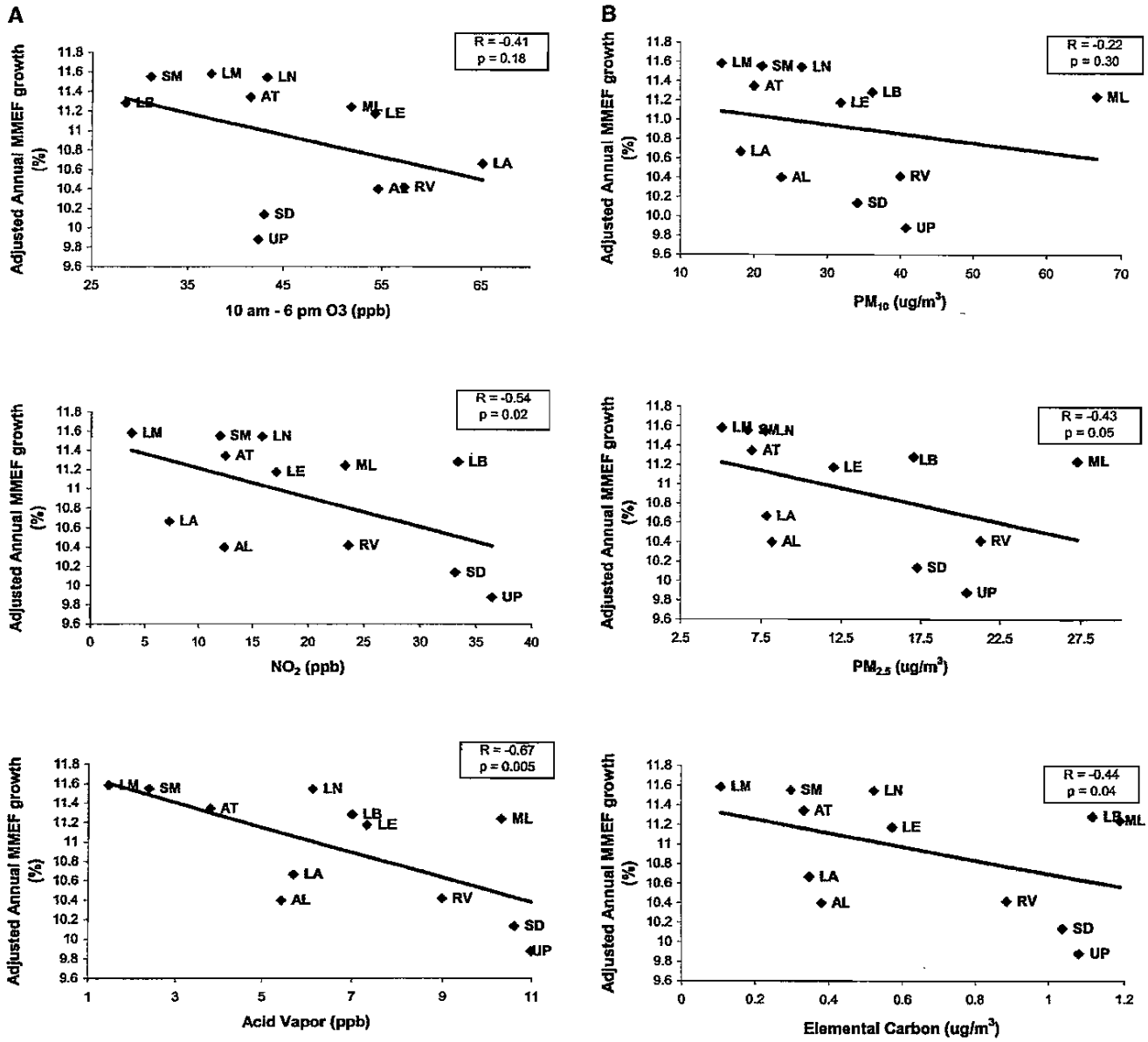


*Figure 2.* Adjusted average annual MMEF growth rates in the 12 communities versus the mean pollutant concentrations over the study period. AL = Alpine; AT = Atascadero; LE = Lake Elsinore; LA = Lake Arrowhead; LN = Lancaster; LM = Lompoc; LB = Long Beach; ML = Mira Loma; RV = Riverside; SD = San Dimas; SM = Santa Maria; UP = Upland.

with lung function growth than did $PM_{10}$, $PM_{10}$–$PM_{2.5}$, and OC. Associations with $PM_{10}$ observed in Cohort 1 were not replicated in Cohort 2. For $PM_{10}$, as well as for $PM_{10}$–$PM_{2.5}$ and OC, Mira Loma had very high levels relative to the other communities (Figures 1 and 2). As an example of how this one community influenced the Cohort 2 results, elimination of Mira Loma from the analysis of MMEF changed the $PM_{10}$-effect estimate from −0.67% ($p = 0.30$, Table 3) to −2.32% ($p = 0.01$). However, we had no *a priori* reason to exclude Mira Loma from the analysis, and we therefore relied on the full 12-community analysis for our inferences. Of the gaseous pollutants, associations with acid vapor and $NO_2$ observed in Cohort 1 were replicated in Cohort 2. However, the associations observed with ozone in Cohort 2 were not previously observed in Cohort 1.

A major source of ambient EC in Southern California is the combustion of diesel fuel (11, 12). The observed associations with EC may therefore indicate a more general association between lung function and exposure to diesel exhaust particles. A previous study of children in the Netherlands also provided evidence of a relationship between diesel exhaust particles and reduced lung function. Specifically, reductions in $FEV_1$, MMEF, and PEFR were associated with exposure to two proxies for diesel emissions, including truck-traffic on nearby roads and levels of black smoke (13). Given that EC largely resides in the fine particle fraction of PM and thus is transported much like a gas, concentrations of EC in any given location will depend on a combination of both local and upwind sources of diesel exhaust particles.

Our finding of an association in Cohort 2 between ozone and PEFR, and between ozone and other lung function measures in children spending more time outdoors, also has some support from prior studies. In a study of Swiss children, expo-

**TABLE 3. DIFFERENCE IN ANNUAL PERCENT GROWTH RATES FROM THE LEAST TO THE MOST POLLUTED COMMUNITY**

| Pollutant[§] | Differences in Growth Rate[†] FVC % (95% CI) | $FEV_1$ % (95% CI) | MMEF % (95% CI) | MMEF/FVC % (95% CI) | PEFR % (95% CI) |
|---|---|---|---|---|---|
| $O_3$, 10 A.M.–6 P.M. | −0.33 (−0.90, 0.24) | −0.55 (−1.27, 0.16) | −0.80 (−1.94, 0.36) | −0.44 (−1.39, 0.52) | −1.21 (−2.06, −0.36)[†] |
| $O_3$ | −0.10 (−0.73, 0.54) | −0.17 (−1.00, 0.67) | −0.09 (−1.41, 1.24) | 0.02 (−0.99, 1.04) | −0.65 (−1.77, 0.49) |
| $NO_2$ | −0.23 (−0.76, 0.29) | −0.48 (−1.12, 0.17) | −1.10 (−2.00, −0.20)* | −0.88 (−1.71, −0.04)* | −0.17 (−1.18, 0.84) |
| Acid vapor | −0.33 (−0.82, 0.17) | −0.63 (−1.21, −0.05)* | −1.28 (−2.16, −0.40)[‡] | −0.96 (−1.77, −0.14)* | −0.74 (−1.62, 0.14) |
| Nitric | −0.36 (−0.84, 0.13) | −0.71 (−1.25, −0.17)[†] | −1.41 (−2.29, −0.53)[‡] | −1.06 (−1.87, −0.24)* | −0.76 (−1.62, 0.12) |
| Formic | −0.39 (−0.89, 0.11) | −0.70 (−1.28, −0.12)* | −1.41 (−2.32, −0.49)[‡] | −1.03 (−1.88, −0.18)* | −0.62 (−1.58, 0.35) |
| Acetic | −0.28 (−0.84, 0.28) | −0.56 (−1.24, 0.13) | −1.17 (−2.14, −0.20)* | −0.89 (−1.78, 0.02) | −0.80 (−1.77, 0.17) |
| $PM_{10}$ | −0.03 (−0.68, 0.62) | −0.21 (−1.04, 0.64) | −0.67 (−1.92, 0.59) | −0.63 (−1.63, 0.38) | −0.42 (−1.60, 0.77) |
| $PM_{2.5}$ | −0.14 (−0.67, 0.40) | −0.39 (−1.06, 0.28) | −0.94 (−1.87, 0.00)* | −0.78 (−1.62, 0.06) | −0.44 (−1.41, 0.55) |
| $PM_{10}$–$PM_{2.5}$ | 0.11 (−0.58, 0.80) | 0.07 (−0.83, 0.98) | −0.19 (−1.60, 1.24) | −0.29 (−1.36, 0.08) | −0.30 (−1.57, 0.99) |
| EC | −0.17 (−0.67, 0.33) | −0.40 (−1.02, 0.23) | −0.92 (−1.78, −0.05)* | −0.74 (−1.53, 0.05) | −0.20 (−1.15, 0.76) |
| OC | 0.01 (−0.67, 0.70) | −0.15 (−1.04, 0.75) | −0.55 (−1.90, 0.83) | −0.55 (−1.61, 0.52) | −0.36 (−1.62, 0.91) |

*Definition of abbreviations*: CI = confidence interval; EC = elemental carbon; MMEF = maximal midexpiratory flow; OC = organic carbon; PEFR = peak expiratory flow rate.
* $p < 0.05$.
† $p < 0.01$.
‡ $p < 0.005$.
§ All pollutant-effect estimates are based on single-pollutant models. Differences in average annual percent growth rates are shown per increase in annual average of 36.6 ppb of $O_3$ (10 A.M.–6 P.M.), 39.8 ppb of $O_3$, 32.7 of $NO_2$, 9.5 ppb of acid vapor, 3.5 ppb of nitric acid, 1.8 ppb of formic acid, 5.0 ppb of acetic acid, 51.5 μg/m³ of $PM_{10}$, 22.2 μg/m³ of $PM_{2.5}$, 29.1 μg/m³ of $PM_{10}$–$PM_{2.5}$, 1.1 μg/m³ of EC, and 10.2 μg/m³ of OC.

sure to outdoor ozone was associated with significant reduction in peak flow after 10 minutes of heavy exercise (14). A similar study of children in the Netherlands observed a negative correlation between post-training peak flow and ozone on the day before the experiment, but it found no association with ozone concentration during exercise (15, 16). In a study of children with mild asthma in Mexico City, decreases in evening peak flow were associated with both same-day and previous-day concentrations of 1-hour maximum ozone (17). A number of summer camp studies, performed in different geographic locations by several research teams, have reported acute decrements in PEFR or $FEV_1$ associated with exposure to ambient $O_3$ (18–24). The longer-term effect of exposure to ambient ozone on children's lung function was investigated by Austrian researchers (2). They obtained repeated PFT over a 3-year period from children in nine Austrian cities and reported associations between ozone and reduced growth in $FEV_1$ and FVC. Collectively, these studies indicate that ozone might have both short- and long-term effects on children's lung function.

Of all the pollutants studied, acid vapor showed the most consistent effect on lung function growth in Cohort 2 and across both cohorts. There are some prior reports on the relationship between acid air pollutants and lung function, although the results are, in general, equivocal. Koenig and coworkers demonstrated reductions in pulmonary function after exposure to high concentrations of nitric acid (25) and with exposure to nitric or sulfuric acid in combination with oxidants (26). However, similarly conducted studies were unable to replicate these results (27, 28). A study of Dutch schoolchildren reported associations between pulmonary function in children and same-day concentrations of nitrous acid that exists in equilibrium with nitric acid (29). In a cross-sectional study of children in 24 North American cities, Raizenne and coworkers (30) showed decrements in FVC and $FEV_1$ with increased exposure to acid sulfate aerosol. No prior studies, though, have investigated the longitudinal effects of acid exposure on the developing lungs of children.

Acid vapor in our study was defined as the sum of nitric, formic, and acetic acids concentrations, each of which was individually associated with decreased lung function growth. The two-pollutant models in Cohort 2 indicated that adjustment for any other pollutant did not qualitatively change the estimated acid effect. Thus, it does not appear that the observed acid effect is simply due to its being correlated with another of the observed pollutants. In fact, the reverse is indicated, specifically that the univariate associations of other pollutants (e.g., $NO_2$, $PM_{2.5}$) with $FEV_1$ and MMEF may be

**TABLE 4. DIFFERENCE IN ANNUAL $FEV_1$ PERCENT GROWTH RATES FROM THE LEAST TO THE MOST POLLUTED COMMUNITY, TWO-POLLUTANT MODELS**

| Main Pollutant[‡] | Adjustment Pollutant $O_3$ (10 A.M.–6 P.M.) | $NO_2$ | Acid Vapor | $PM_{10}$ | $PM_{2.5}$ | EC |
|---|---|---|---|---|---|---|
| $O_3$, 10 A.M.–6 P.M | **−0.55** | −0.71* | −0.38 | −0.54 | −0.50 | −0.57 |
| $NO_2$ | −0.62* | **−0.48** | 0.21 | −0.64 | −0.44 | −0.64 |
| Acid vapor | −0.53 | −0.80 | **−0.63*** | −1.34[†] | −1.27* | −1.43* |
| $PM_{10}$ | −0.13* | 0.29 | 1.10 | **−0.21** | 2.40* | 0.91 |
| $PM_{2.5}$ | −0.33 | −0.05 | 0.76 | −2.26* | **−0.39** | 0.01 |
| EC | −0.42 | 0.16 | 0.86 | −1.01 | −0.41 | **−0.40** |

*Definition of abbreviations*: EC = elemental carbon; $PM_{10}$ = particles with aerodynamic diameter less than 10 μm.
* $p < 0.05$.
† $p < 0.01$.
‡ Each row gives effect estimates for the indicated pollutant after adjustment for the pollutant listed at the top of the column. Boldface estimates are from the single-pollutant models shown in Table 3. *See* Table 3 footnote for the description of units.

**TABLE 5. DIFFERENCE IN ANNUAL MMEF PERCENT GROWTH RATES FROM THE LEAST TO THE MOST POLLUTED COMMUNITY, TWO-POLLUTANT MODELS**

| Main Pollutant[§] | Adjustment Pollutant | | | | | |
|---|---|---|---|---|---|---|
| | $O_3$ (10 A.M.–6 P.M.) | $NO_2$ | Acid Vapor | $PM_{10}$ | $PM_{2.5}$ | EC |
| $O_3$, 10 A.M.–6 P.M | **−0.80** | −1.11* | −0.40 | −0.73 | −0.65 | −0.83 |
| $NO_2$ | −1.31† | **−1.10*** | 0.03 | −1.30* | −0.96 | −1.45* |
| Acid vapor | −1.18* | −1.31 | **−1.28‡** | −2.33† | −2.14* | −2.44* |
| $PM_{10}$ | −0.57 | 0.36 | 1.63 | **−0.67** | 3.98* | 1.38 |
| $PM_{2.5}$ | −0.86† | −0.18 | 1.02 | −3.97 | **−0.94*** | −0.20 |
| EC | −0.94* | 0.36 | 1.25 | −1.85* | −0.74† | **−0.92*** |

*Definition of abbreviations*: EC = elemental carbon; MMEF = maximal midexpiratory flow.
* $p < 0.05$.
† $p < 0.01$.
‡ $p < 0.005$.
§ Each row gives effect estimates for the indicated pollutant after adjustment for the pollutant listed at the top of the column. Boldface estimates are from the single-pollutant models shown in Table 3. *See* Table 3 footnote for the description of units.

due to the correlation of these pollutants with acid vapor. However, we cannot rule out the possibility that some pollutant(s) we did not measure is responsible for the observed health effects and that acid vapor is simply our best marker of that pollutant or pollutant mixture. More specifically, acid vapor concentration may be our best indicator of downwind transport coupled with atmospheric chemical processes. This conjecture is supported by the observation that acid vapor is the pollutant we studied that most clearly distinguishes the four communities downwind of the greater Los Angeles area (Mira Loma, Riverside, San Dimas, Upland) from the remaining eight communities (*see* Figure E1 or Figure 1). Whether acid vapor is causally related to reduced lung function development or whether it is simply our best marker for another causative substance or mixture, this pollutant deserves further study.

Generally speaking, children in a community with high pollution will be more likely than children in a lower-pollution community to be exposed to short-term episodes of very high concentrations of pollutants. In southern California, concentrations of most of the pollutants we studied are highest in the afternoon hours, and therefore children who spend time outdoors during this time may receive a substantially higher dose to their lungs on a polluted day than children who remain indoors. At least 70% of the subjects reported having a home air conditioner in our polluted communities, a factor that can further increase the discrepancy between indoor and outdoor concentrations of ozone and some other pollutants. Prior reports, some of which have been summarized previously in this article, indicate that short-term exposure to high pollution can have acute effects on respiratory symptoms and lung function. A study of children in Poland has shown a link between repeated respiratory symptoms and reduced lung function growth (31). Our observations of reduced lung function growth with increasing annual average pollution level may thus be a consequence of repeated acute respiratory events after short-term increases in pollution levels. Our finding of larger deficits in children who reported spending more time outdoors in the afternoon adds some support to this possibility. However, additional study is needed to investigate the temporal relationship between acute respiratory events and lung function development.

In summary, the observed associations in this second fourth-grade cohort of the CHS generally replicated the findings from the first CHS fourth-grade cohort. Analysis of Cohort 2 showed the strongest associations with acid vapor. The observed pollutant-effect estimates were larger for MMEF than for the other PFT measures. This finding, in conjunction with significant associations between pollution and the volume-corrected measure, MMEF/FVC, indicates that long-term pollution exposure may affect the development of small airways in the lung. Further follow-up of CHS participants will allow determination of whether pollution-related deficits in lung function growth persist into adulthood, resulting in lower maximal attained lung function, and perhaps, leading to increased risk of respiratory illness.

**TABLE 6. DIFFERENCE IN ANNUAL PERCENT GROWTH RATES FROM THE LEAST TO THE MOST POLLUTED COMMUNITY: COMPARISON OF COHORTS 1 AND 2**

| PFT | Pollutant† | Cohort 1 (*n* = 1,457‡, %, 95% CI) | Cohort 2 (*n* = 1,678‡, %, 95% CI) |
|---|---|---|---|
| FVC | $O_3$, 10 A.M.–6 P.M. | −0.22 (−0.77, 0.33) | −0.33 (−0.90, 0.24) |
| | $NO_2$ | −0.46 (−0.92, 0.00) | −0.23 (−0.76, 0.29) |
| | Total acid | −0.55 (−0.97, −0.11)* | −0.33 (−0.82, 0.17) |
| | $PM_{10}$ | −0.60 (−1.18, −0.01)* | −0.03 (−0.68, 0.62) |
| | $PM_{2.5}$ | −0.42 (−0.86, 0.03) | −0.14 (−0.67, 0.40) |
| | EC | −0.49 (−0.88, −0.09)* | −0.17 (−0.67, 0.33) |
| $FEV_1$ | $O_3$, 10 A.M.–6 P.M. | −0.32 (−1.14, 0.50) | −0.55 (−1.27, 0.16) |
| | $NO_2$ | −0.66 (−1.34, 0.02) | −0.48 (−1.12, 0.17) |
| | Total acid | −0.82 (−1.44, −0.19)* | −0.63 (−1.21, −0.05)* |
| | $PM_{10}$ | −0.94 (−1.78, −0.10)* | −0.21 (−1.04, 0.64) |
| | $PM_{2.5}$ | −0.63 (−1.28, 0.02) | −0.39 (−1.06, 0.28) |
| | EC | −0.71 (−1.30, −0.12)* | −0.40 (−1.02, 0.23) |
| MMEF | $O_3$, 10 A.M.–6 P.M | −0.43 (−1.64, 0.80) | −0.80 (−1.94, 0.36) |
| | $NO_2$ | −0.92 (−1.95, 0.12) | −1.10 (−2.00, −0.20)* |
| | Total acid | −1.16 (−2.12, −0.19)* | −1.28 (−2.16, −0.40)*** |
| | $PM_{10}$ | −1.41 (−2.61, −0.21)* | −0.67 (−1.92, 0.59) |
| | $PM_{2.5}$ | −0.94 (−1.88, 0.01) | −0.94 (−1.87, 0.00)* |
| | EC | −1.07 (−1.94, −0.19)* | −0.92 (−1.78, −0.05)* |
| PEFR | $O_3$, 10 A.M.–6 P.M | −0.36 (−1.34, 0.63) | −1.21 (−2.06, −0.36)** |
| | $NO_2$ | −0.82 (−1.62, −0.02)* | −0.17 (−1.18, 0.84) |
| | Total acid | −1.00 (−1.75, −0.25)** | −0.74 (−1.62, 0.14) |
| | $PM_{10}$ | −1.27 (−2.15, −0.37)** | −0.42 (−1.60, 0.77) |
| | $PM_{2.5}$ | −0.82 (−1.55, −0.09)* | −0.44 (−1.41, 0.55) |
| | EC | −0.89 (−1.57, −0.20)* | −0.20 (−1.15, 0.76) |

*Definition of abbreviations*: CI = confidence interval; EC = elemental carbon; MMEF = maximal midexpiratory flow; PEFR = peak expiratory flow rate; PFT = pulmonary function test.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.005$.
† All pollutant-effect estimates are based on single-pollutant models. Differences in average annual percent growth rates are shown per increase in annual average of 36.6 ppb of $O_3$ (10 A.M.–6 P.M.), 39.8 ppb of $O_3$, 32.7 of $NO_2$, 9.5 ppb of acid vapor, 3.5 ppb of nitric acid, 1.8 ppb of formic acid, 5.0 ppb of acetic acid, 51.5 $\mu g/m^3$ of $PM_{10}$, 22.2 $\mu g/m^3$ of $PM_{2.5}$, 29.1 $\mu g/m^3$ of $PM_{10}$–$PM_{2.5}$, 1.1 $\mu g/m^3$ of EC, and 10.2 $\mu g/m^3$ of OC.
‡ Cohort 1 includes children enrolled in 1993 as fourth graders and followed through 1997. Cohort 2 includes children enrolled in 1996 as fourth graders and followed through 2000. The results shown for Cohort 2 are equivalent to those shown in Table 3.

**TABLE 7. DIFFERENCE IN ANNUAL PERCENT GROWTH RATES FROM THE LEAST TO THE MOST POLLUTED COMMUNITY**

| | | Cohort 1 | | | | Cohort 2 | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | More Outdoors† | | Less Outdoors | | More Outdoors† | | Less Outdoors | |
| | | Difference in Growth‡ | | Difference in Growth | | Difference in Growth‡ | | Difference in Growth | |
| PFT | Pollutant‡ | % | *(95% CI)* | % | *(95% CI)* | % | *(95% CI)* | % | *(95% CI)* |
| FVC | $O_3$, 10 A.M.–6 P.M. | −0.02 | (−0.70, 0.66) | −0.05 | (−0.55, 0.45) | −0.69 | (−1.26, −0.11)* | −0.07 | (−0.93, 0.80) |
| | $NO_2$ | −0.45 | (−1.01, 0.12) | −0.14 | (−0.63, 0.36) | −0.44 | (−0.99, 0.12) | −0.15 | (−0.92, 0.62) |
| | Acid vapor | −0.43 | (−1.01, 0.15) | −0.25 | (−0.75, 0.25) | −0.63 | (−1.13, −0.13)* | −0.12 | (−0.88, 0.64) |
| | $PM_{10}$ | −0.35 | (−1.10, 0.42) | −0.52 | (−1.10, 0.07) | −0.44 | (−1.11, 0.22) | 0.32 | (−0.60, 1.24) |
| | $PM_{2.5}$ | −0.23 | (−0.80, 0.35) | −0.32 | (−0.76, 0.12) | −0.47 | (−0.99, 0.06) | 0.14 | (−0.65, 0.93) |
| | EC | −0.43 | (−0.94, 0.08) | −0.28 | (−0.73, 0.16) | −0.44 | (−0.94, 0.08) | 0.01 | (−0.73, 0.75) |
| $FEV_1$ | $O_3$, 10 A.M.–6 P.M. | −0.31 | (−1.44, 0.83) | −0.06 | (−0.71, 0.60) | −0.83 | (−1.66, 0.00) | −0.35 | (−1.25, 0.56) |
| | $NO_2$ | −0.96 | (−1.83, −0.08)* | −0.36 | (−0.97, 0.26) | −0.82 | (−1.56, −0.08)* | −0.21 | (−1.03, 0.61) |
| | Acid vapor | −1.10 | (−1.94, −0.25)* | −0.44 | (−1.07, 0.20) | −1.01 | (−1.65, −0.38)*** | −0.31 | (−1.11, 0.49) |
| | $PM_{10}$ | −1.12 | (−2.24, 0.01) | −0.65 | (−1.39, 0.09) | −0.63 | (−1.60, 0.35) | 0.20 | (−0.80, 1.21) |
| | $PM_{2.5}$ | −0.74 | (−1.63, 0.14) | −0.49 | (−1.05, 0.07) | −0.80 | (−1.51, −0.08)* | −0.01 | (−0.86, 0.84) |
| | EC | −0.97 | (−1.72, −0.21)* | −0.40 | (−0.97, 0.17) | −0.74 | (−1.44, −0.03)* | −0.09 | (−0.87, 0.71) |
| MMEF | $O_3$, 10 A.M.–6 P.M. | −0.67 | (−2.54, 1.23) | 0.28 | (−1.09, 1.66) | −0.58 | (−2.09, 0.95) | −0.97 | (−2.52, 0.61) |
| | $NO_2$ | −1.59 | (−2.95, −0.20)* | −0.72 | (−2.09, 0.66) | −1.48 | (−2.84, −0.11)* | −0.51 | (−1.92, 0.93) |
| | Acid vapor | −1.83 | (−3.20, −0.43)* | −0.66 | (−2.07, 0.76) | −1.35 | (−2.65, −0.03)* | −0.99 | (−2.28, 0.32) |
| | $PM_{10}$ | −2.05 | (−3.69, −0.37)* | −0.89 | (−2.53, 0.78) | −0.54 | (−2.14, 1.09) | −0.64 | (−2.36, 1.12) |
| | $PM_{2.5}$ | −1.46 | (−2.70, −0.20)* | −0.71 | (−1.96, 0.55) | −0.95 | (−2.26, 0.39) | −0.74 | (−2.16, 0.70) |
| | EC | −1.74 | (−2.98, −0.49)** | −0.57 | (−1.83, 0.70) | −1.03 | (−2.29, 0.25) | −0.54 | (−1.89, 0.82) |
| PEFR | $O_3$, 10 A.M.–6 P.M. | −0.94 | (−2.48, 0.63) | 0.31 | (−0.79, 1.42) | −1.62 | (−2.93, −0.29)* | −0.87 | (−2.09, 0.37) |
| | $NO_2$ | −1.42 | (−2.52, −0.30)* | −0.36 | (−1.46, 0.75) | −0.52 | (−1.98, 0.96) | 0.38 | (−0.77, 1.55) |
| | Acid vapor | −1.74 | (−2.82, −0.66)*** | −0.32 | (−1.45, 0.82) | −1.27 | (−2.51, −0.01)* | −0.01 | (−1.18, 1.17) |
| | $PM_{10}$ | −1.81 | (−3.11, −0.49)** | −0.87 | (−2.19, 0.46) | −0.71 | (−2.41, 1.03) | 0.22 | (−1.21, 1.66) |
| | $PM_{2.5}$ | −1.33 | (−2.34, −0.31)* | −0.47 | (−1.47, 0.54) | −0.73 | (−2.12, 0.69) | 0.13 | (−1.08, 1.35) |
| | EC | −1.36 | (−2.34, −0.37)** | −0.41 | (−1.42, 0.61) | −0.52 | (−1.88, 0.86) | 0.41 | (−0.69, 1.52) |

*Definition of abbreviations*: CI = confidence interval; EC = elemental carbon; MMEF = maximal midexpiratory flow; PEFR = peak expiratory flow rate; PFT = pulmonary function test.

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.005$.

† More/less outdoors is based on reported time spent outdoors during weekday afternoons. Subjects were split into the two groups on the basis of the median of reported time outdoors with each cohort.

‡ All pollutant-effect estimates are based on single-pollutant models. Differences in average annual percent growth rates are shown per increase in annual average of 36.6 ppb of $O_3$ (10 A.M.–6 P.M.), 39.8 ppb of $O_3$, 32.7 of $NO_2$, 9.5 ppb of acid vapor, 3.5 ppb of nitric acid, 1.8 ppb of formic acid, 5.0 ppb of acetic acid, 51.5 μg/m³ of $PM_{10}$, 22.2 μg/m³ of $PM_{2.5}$, 29.1 μg/m³ of $PM_{10}$–$PM_{2.5}$, 1.1 μg/m³ of EC, and 10.2 μg/m³ of OC.

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# The Effects of Ambient Air Pollution on School Absenteeism Due to Respiratory Illnesses

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We investigated the relations between ozone ($O_3$), nitrogen dioxide ($NO_2$), and respirable particles less than 10 $\mu$m in diameter ($PM_{10}$) and school absenteeism in a cohort of 4th-grade school children who resided in 12 southern California communities. An active surveillance system ascertained the numbers and types of absences during the first 6 months of 1996. Pollutants were measured hourly at central-site monitors in each of the 12 communities. To examine acute effects of air pollution on absence rates, we fitted a two-stage time-series model to the absence count data that included distributed lag effects of exposure adjusted for long-term pollutant levels. Short-term change in $O_3$, but not $NO_2$ or $PM_{10}$, was associated with a substantial increase in school absences from both upper and lower respiratory illness. An increase of 20 ppb of $O_3$ was associated with an increase of 62.9% [95% confidence interval (95% CI) = 18.4–124.1%] for illness-related absence rates, 82.9% (95% CI = 3.9–222.0%) for respiratory illnesses, 45.1% (95% CI = 21.3–73.7%) for upper respiratory illnesses, and 173.9% (95% CI = 91.3–292.3%) for lower respiratory illnesses with wet cough. The short-term effects of a 20-ppb change of $O_3$ on illness-related absenteeism were larger in communities with lower long-term average $PM_{10}$ [223.5% (95% CI = 90.4–449.7)] compared with communities with high average levels [38.1% (95% CI = 8.5–75.8)]. Increased school absenteeism from $O_3$ exposure in children is an important adverse effect of ambient air pollution worthy of public policy consideration. (Epidemiology 2001;12:43–54)

**Keywords: air pollution, ozone, respiratory illnesses and children, school absenteeism.**

Ambient air pollutants including ozone ($O_3$), nitrogen dioxide ($NO_2$), and respirable particles less than 10 $\mu$m in diameter ($PM_{10}$) contribute to the occurrence of respiratory symptoms and diseases including increased occurrence and severity of symptoms, transient changes in lung function, and increased respiratory infections, more visits to physicians and emergency rooms and increased hospital admissions, and changes in lung function and increased mortality.[1–5] Consideration of a broader group of outcomes, such as school absenteeism, provides a more comprehensive assessment of the adverse impact of ambient air pollution.[6,7]

Illness-related school absenteeism is an important but insufficiently studied outcome in children, a group identified as especially sensitive to the adverse effects of ambient air pollution.[8] Illness-related absences are common events that represent a broad spectrum of morbidity from mild transient illnesses to the most severe and prolonged illnesses that require emergency room visits or hospital admissions.[9] Although most absences are associated with illnesses at the low end of the morbidity spectrum, an absence indicates an illness of sufficient severity to affect the child's daily functioning, as well as child and family coping strategies.[9–13]

Population-based studies show that absence rates vary by school, age, grade, and gender, and are affected by family structure, function, and other social factors.[14,15] Although the non-health-related influences on absenteeism limit its usefulness as a measure of the adverse effects of air pollution, the majority of school absences are illness related and attributable to either respiratory infections or gastroenteritis, suggesting that illness is the dominant factor for school absenteeism.[10,14] Because the

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effects of air pollution on school absences are likely to be due to increases in respiratory illnesses, respiratory illness-related absenteeism can be an important and relatively specific integrative outcome for the assessment of the effects of air pollution on children.

Most research on the effects of air pollution on children's health has focused on self-reported symptoms, indices of respiratory infections derived from clinical visits, medical records reviews, and lung function as outcome measures.[6,16] Few studies have examined the effects of ambient air pollution on school absenteeism, and none has examined the effects on respiratory-related absences in school-aged children residing in communities with large variations in pollutant levels.

The Children's Health Study (CHS) offers an opportunity to investigate the effects of three ambient pollutants, $O_3$, $PM_{10}$, and $NO_2$, on school absenteeism with a focus on respiratory illness-related absences.[17] We conducted a substudy within the CHS cohort, the Air Pollution and Absence Study, and examined data on type-specific absence incidence collected by an active surveillance system for a cohort of 4th-grade school children 9–10 years of age who attended schools in the 12 CHS study communities during January through June 1996.

## Subjects and Methods

### Study Design

The CHS is a 10-year longitudinal study that includes school children who reside in 12 communities within a 200-mile radius of Los Angeles that were selected to represent the broadest range in concentration of the ambient pollutants of interest. Details on the design, site selection, subject recruitment, and assessment of health effects are reported elsewhere.[17] In this report, we focus on school absences among 2,081 children in the 4th grade during the first 6 months of 1996.

### Participant Characteristics

Sociodemographic information, indoor exposures, and medical histories were obtained from questionnaires completed by parents or guardians at study entry in the fall of 1995. Environmental tobacco smoke (ETS) exposure was classified as exposure to a current household smoker or not. The subset of participants with asthma was defined using parent-reported history of physician-diagnosed asthma. Children with wheezing were defined as having any lifetime history of wheezing. Information regarding the number of hours spent outdoors over a 1-week period was collected by self-administered questionnaire. Children were stratified into "more outdoors" or "less outdoors" groups on the basis of whether they were above or below the median number of hours spent outside (11.25 hours).

### Absence Surveillance

We collected school absence reports from the 27 elementary schools attended by the newly recruited 4th-grade children for the period January 1 through June 30, 1996. Of the 2,081 children in the 4th-grade group, 2,068 were eligible for the absence surveillance because they were enrolled in the CHS at the beginning of the surveillance period. Of these 2,068 children, we excluded 135 from the analysis for the following reasons: 32 withdrew from the study, 90 changed schools during the study period, and 13 did not have absence data because of administrative errors.

Daily absence information was collected using two methods depending on school confidentiality policies. In 12 schools, attendance reports for entire classrooms were collected, and study staff identified absences for participating students. In the remaining 15 schools, school staff members supplied subject-specific absence reports based on lists of subjects provided to them at the beginning of the surveillance period. Study staff requested that absence reports be completed every 2–4 weeks, with the interval depending on the availability of personnel and electronic data systems at individual schools. We defined an absence as a day or an adjacent series of school days in which a participant did not attend school when the school was in session. Over the period of study, we ascertained 8,971 absences.

We established an active surveillance system to collect information about the reasons for absences; we categorized absences as illness-related and non-illness-related (these included injuries) and classified illness-related absences into gastrointestinal (GI) and respiratory categories. School reports classified absences with nonstandard codes including indicators for non-illness-related absences. Non-illness-related absences were not investigated by telephone interviews. Using school reports, study staff assigned daily absence reports to one of two categories: (1) non-illness related and (2) potentially illness related. To ensure adequate parental recall of events associated with the absence of interest, interviews were conducted only for absences that were reported within 4 weeks of occurrence. Of the 3,294 absences reported within 4 weeks, 536 were classified as non-illness absences on the basis of school reports, and 2,758 absences required telephone follow-up.

Telephone interviews were conducted in English or Spanish by trained interviewers using a standardized protocol. Parents were contacted after each absence that was reported within 4 weeks to inquire whether the absence was illness related and if so, what the symptoms were; what the physician diagnoses were, if any; and what medications were used for the reported illness. The interviewers used a list of symptoms to categorize respiratory illnesses (runny nose and sneezing, fever, sore throat, cough, wet cough, dry cough, earache, wheezing, and asthma attack) in addition to stomach problems; head and muscle aches with fatigue; rash or skin problems; watery, itchy, or burning eyes; allergies; and other symptoms. Repeat interviews were conducted for approximately 5% of absences for quality-control purposes.

Each illness-related absence was classified as respiratory or nonrespiratory on the basis of the reported symptoms. We defined a respiratory illness as an illness that included one or more of the following symptoms: runny

nose/sneezing, sore throat, cough (any, wet, or dry), earache, wheezing, or asthma attack. Respiratory absences were further classified into non-mutually exclusive categories of upper respiratory illness and/or as one of two types of lower respiratory illness (LRI): LRI with wet cough or LRI with wet cough/wheeze/asthma. We defined an upper respiratory illness as a respiratory illness with one or more of the following symptoms: runny nose/sneezing, sore throat, and earache. GI illnesses included illnesses with "stomach problems" such as vomiting and diarrhea as one of the reported symptoms.

### Absence Incidence Rates

We categorized each absence day as an incident or prevalent absence day using absence reports and school calendars to identify the days each school was in session. We defined an incident absence as an absence that followed attendance on the preceding school day. We defined a prevalent absence day as an absence that occurred after an absence on the preceding school day. The date of an absence occurrence was assigned to the incident day of each series of absence days.

We used the daily number of incident absences in each community and the corresponding daily number of children at risk for an absence in each community to calculate daily community-specific incident absence rates. We defined the number of students attending a school as the number of participants enrolled in a school on a day that the school was in session less the number of prevalent absences. We calculated daily community-specific incidence rates of absence by pooling the data from the reporting schools in each community and dividing the community-specific number of incident absences by the number of students attending schools in that community on the day of interest. The average incidence rate for school absences was computed for each community by averaging daily rates and for the entire cohort by averaging across days and communities. Stratified rates (for example, by asthma status) were calculated by identifying the number of absences and number of students at risk within each stratum and calculating daily community-specific rates and average rates as described.

On the basis of data collected by the active surveillance system, absences were divided into three mutually exclusive outcomes: non-illness-related absences, illness-related absences, and absences of unknown type (due to failure to obtain necessary classification information). Because some absences were of unknown type, the type-specific absence incidence rates were adjusted for ascertainment failure. To adjust the type-specific incident absence rates, we calculated a daily community-specific information success ratio, which we defined as the daily proportion of timely absence reports in each community for which sufficient information was obtained to assign the absence as illness related or non-illness related. This success ratio was then smoothed over time using a very rough smoother (using 10 degrees of freedom). The smoothing was intended to reduce the random fluctuation due to the limited number of events on each day within a community but in such a way that it did not substantially alter the overall trend in the data or the observed values. A symptom-specific incidence rate corrected for ascertainment is of the form: (number of incident cases)/(number at risk × smoothed success ratio).

### Assessment of Air Pollution Levels

Levels for $O_3$, $PM_{10}$, and $NO_2$ were measured continuously with hourly averaging at central-site monitors in each of the 12 communities.[18] We calculated the daily 1-hour maximum $O_3$, the 24-hour average of $O_3$, and the 10 am–6 pm average of $O_3$, as well as the 24-hour averages of $PM_{10}$ and $NO_2$. We focused on the 10 am–6 pm average of $O_3$ because it is an index of exposure during the temporal peak of ozone and outdoor activity. The 24-hour averages of $PM_{10}$ and $NO_2$ were used because they lack the temporal peak exhibited by $O_3$. The monitoring program also reported daily 24-hour average, 24-hour maximum, and 24-hour minimum temperatures at each of the 12 monitoring locations. To assess the effects of long-term average levels of $O_3$, $PM_{10}$, and $NO_2$ on acute effects, we divided communities into high and low groups for each pollutant on the basis of its ranking on average levels for 1995. The high and low groups included the same communities for $PM_{10}$ and $NO_2$.

### Statistical Methods

To examine acute effects of each air pollutant on the rate of absences, we fitted a two-stage time-series model to the absence count data.[19–23] Letting $\mu_c(t)$ denote the expectation of these absence counts and $R_c(t)$ denote the number of children at risk in community $c$ on day $t$, the first-stage Poisson log-linear model has the form

$$\text{Stage 1: } \ln[\mu_c(t)] = \ln(R_c(t)) + s(t) + b_c + d_c[X_c(t) - X_c] + \gamma Z_c(t)$$

where $b_c$ denotes the average absence rate in community $c$, adjusted for the effects of time-dependent covariates $Z_c(t)$ (for example, temperature, day of the week), and $d_c$ is the within-community slope of the regression of change in daily absence rates with change in daily pollution $X_c(t)$ centered at the 6-month average for the study period $X_c$. The centering assumes a log-linear relation between the pollutants and absences. Here, $s(t)$ denotes a smooth function of time to account properly for autocorrelation and long- and short-term time trends in the multiple time series of counts. We use 5 degrees of freedom for the 6-month period to remove any temporal cycles of up to 2 weeks.[20] The first-stage model was also adjusted for day of the week (with Friday as the reference day) and temperature (24-hour average, daily minimum, and daily maximum). The offset term, $R_c(t)$, in the Poisson model was adjusted by using a smoothed version of the success ratio as described above.

Because the effects of pollutant exposure on a given day are likely to occur over several days, we fit models

that allowed acute effects to be distributed over time. To account for a lag structure of the pollution effect, we modified the first-stage model by including community-specific polynomial distributed lag terms[24–27] leading to a model of the form:

$$\ln[\mu_c(t)] = \ln[R_c(t)] + s(t) + b_c + \gamma Z_c(t) + \Sigma_k g_{ck} \Sigma_j [X_c(t-j) - X_c] j^k$$

where $j = 1, ..., L$, $d_{cj} = \Sigma_k g_{ck} j^k$, and $k = 0, ..., D$, implying that the effects of each of the previous $L$ days are distributed over subsequent days following a polynomial function of degree $D$. Appropriate values for $L$ and $D$ are optimally selected by comparing the Akaike Information Criterion[22,28] of the models based on a grid of $L$ and $D$ values assuming the same $D$ and $L$ values for all communities. This assumption is based on biological considerations indicating that the effects of pollutants should have the same lag structure in different communities in the Los Angeles region. The quantity $d_{cj} = \Sigma_k g_{ck} j^k$ is then interpretable as the polynomially smoothed estimate of the effect of air pollution on lagged $j$ days, and their sum $d_c = \Sigma_j d_{cj}$ is the overall effect of pollution over the entire lag period. The estimates of $d_{cj}$ and their variance estimates are then recovered through the explicit relation between $d_{cj}$ and $g_{ck}$.[26]

The first-stage regression is followed by an ecologic linear regression model given by:

$$\text{Stage 2: } d_c = \delta_0 + \delta X_c + \eta_c$$

The stage 2 regression takes the sum of the lagged community-specific effects, $d_c$, and the appropriate variance estimates from stage 1. The parameter $\delta_0$, the mean of the within-community slopes $d_c$, serves as an aggregated acute-effect estimate and is the quantity of primary interest for testing acute effects of air pollutants. Because long-term pollution levels may affect responses to acute changes in exposure level, the stage 2 model includes long-term average levels of any of the pollutants of interest and allows modification of the community-specific slopes for the acute effects by long-term average pollution levels. The parameter $\delta$ characterizes the modifying effect of the long-term average pollution levels on the relation between change in absences and change in daily within-community pollution levels. Note that we use the deviation of the daily exposure values, $X_c(t)$, from $X_c$ in the first-stage model to make the within- and between-community comparisons of pollution effects independent. The second-stage "ecologic" regression is weighted by the inverses of the variances of $d_c$.

Using this framework, we fitted separate models for three pollutants; $O_3$ (24-hour average, daily maximum, and 10 am–6 pm daily average), $PM_{10}$ (24-hour average), and $NO_2$ (24-hour average). To account for effects of long-term ambient pollutant levels, regression models were fitted and the overall summary of acute effect of a pollutant across communities was estimated, adjusted for the 1995 community-specific average levels of a pollutant. The estimate of $\delta_0$ provides an overall summary of the acute effects from January through June 1996, adjusted for 1995 average levels of pollution or any other community-specific ecologic factor.

To assess further whether long-term average pollutant levels modify the acute effects of a pollutant, stratified models were fit using categories of high- and low-pollution communities. For any given number of strata, $S$, the stage 2 model becomes $d_c = \delta_{0s} + \eta_c$, where $s = 1, \ldots S$ and summary estimates are obtained as above. Strata of communities were formed on the basis of rankings using 1995 average pollution levels. We divided communities into high and low based on long-term average levels of $O_3$ and $PM_{10}$ or $NO_2$.

## Results

The distribution of sociodemographic characteristics, medical conditions, ETS exposure, and outdoor activity varied among the communities (Table 1). The average daily incidence rate for all types of absences combined was 3.07 per 100 student-days based on an average daily attendance of 1,502 students (Table 2). Average daily absence rates were highest in Lake Gregory and lowest in Upland. Although the method of absence reporting by schools varied by community (Table 1), the method of school attendance reporting did not appear to have a large influence on incidence rates.

The subset of absences that was reported in a timely enough manner to be eligible for the active surveillance system was an unbiased sample of absences occurring on all days (Table 2). The distribution of determinants of absences and the average daily rates for all types of absences on days that were reported within 4 weeks did not differ substantially from the distribution and average rates on days ascertained over the period of study. The crude average daily rates per 100 participants were 1.07 for non-illness-related absences, 1.34 for illness-related absences, and 0.61 for absences of unknown type (Table 3). The daily information success ratio averaged 0.81, and exceeded 0.72, for all subgroups.

The ascertainment-adjusted daily rate for illness-related absences was higher than for non-illness-related absences for all participants combined (Table 4). Lake Gregory had the highest adjusted daily rate for illness-related absences, and Long Beach had the lowest rate. Illness-related absences were primarily due to respiratory illnesses, most of which had upper respiratory symptoms (Table 4). Adjusted daily rates of absences for respiratory illness, upper respiratory illness, LRI with wet cough/wheeze/asthma, and LRI with wet cough varied among communities and among ethnic and education groups. Rates of absences for respiratory illness and upper respiratory illness were twice as high in Lake Gregory compared with rates in Long Beach. Children with asthma, wheezing, and ETS exposure had higher absence rates for all categories of respiratory illness than children without asthma, wheezing, or ETS exposure. Adjusted absence rates for GI illness did not vary as substantially as rates for respiratory illness by children's asthma status, wheezing status, or ETS exposure (Table 4). Absences

TABLE 1. Percentage Distributions of Sociodemographic Characteristics and Selected Medical History and Exposures among Participants, Air Pollution, and Absence Study, January through June 1996

| Community Reporting | N | Males | Race/Ethnicity | | | | | Parent Education* | | | | Conditions | | | | Reporting Method† | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | White | Hispanic | African American | Asian | Other Race | <12th Grade | 12th Grade | Some College/ Technical School | 4 Years College | Postgraduate | Asthma | Wheeze | ETS | Outdoor Activity >11.25 Hours | Subject-Specific Reporting | Whole Grade |
| Alpine | 177 | 49.7 | 73.4 | 20.9 | 0 | 0.6 | 4.5 | 7.9 | 20.3 | 49.2 | 10.7 | 9.0 | 13.6 | 33.9 | 16.4 | 57.6 | 0 | 100.0 |
| Lake Elsinore | 171 | 47.4 | 52.0 | 33.9 | 2.3 | 2.9 | 6.4 | 18.1 | 21.1 | 38.0 | 11.1 | 4.1 | 11.1 | 31.6 | 21.1 | 45.0 | 45.6 | 54.4 |
| Lake Gregory | 164 | 52.4 | 71.3 | 22.0 | 0.6 | 0 | 5.5 | 9.8 | 19.5 | 50.6 | 7.3 | 8.5 | 14.6 | 35.4 | 29.9 | 29.9 | 24.4 | 75.6 |
| Lancaster | 176 | 47.2 | 49.4 | 31.3 | 10.8 | 2.3 | 5.1 | 17.6 | 18.2 | 44.9 | 6.8 | 8.0 | 16.5 | 34.7 | 24.4 | 52.3 | 100.0 | 0 |
| Lompoc | 166 | 49.4 | 44.0 | 36.1 | 6.6 | 9.0 | 4.2 | 12.7 | 19.3 | 48.8 | 9.6 | 5.4 | 10.8 | 29.5 | 19.9 | 33.1 | 34.3 | 65.7 |
| Long Beach | 158 | 54.4 | 32.3 | 23.4 | 21.5 | 13.9 | 8.2 | 10.8 | 19.6 | 39.2 | 13.3 | 12.0 | 13.9 | 27.8 | 20.3 | 38.0 | 66.5 | 33.5 |
| Mira Loma | 152 | 48.0 | 40.8 | 52.6 | 2.0 | 1.3 | 2.6 | 27.0 | 24.3 | 31.6 | 7.9 | 1.3 | 14.5 | 34.2 | 24.3 | 42.8 | 100.0 | 0 |
| Riverside | 152 | 49.3 | 40.1 | 40.8 | 10.5 | 1.3 | 5.9 | 15.1 | 23.0 | 32.9 | 9.2 | 17.1 | 11.8 | 26.3 | 12.5 | 52.6 | 0 | 100.0 |
| San Dimas | 162 | 48.8 | 48.8 | 35.2 | 1.9 | 8.6 | 5.6 | 6.2 | 15.4 | 53.7 | 10.5 | 9.3 | 18.5 | 30.9 | 17.3 | 38.9 | 0 | 100.0 |
| Atascadero | 157 | 56.1 | 72.6 | 17.2 | 1.9 | 1.3 | 7.0 | 4.5 | 17.8 | 50.3 | 8.9 | 17.2 | 19.7 | 43.3 | 13.4 | 50.3 | 0 | 100.0 |
| Santa Maria | 156 | 49.4 | 22.4 | 62.8 | 0.6 | 7.1 | 3.2 | 21.2 | 22.4 | 30.8 | 7.1 | 5.1 | 12.2 | 19.2 | 12.8 | 34.6 | 100.0 | 0 |
| Upland | 144 | 47.2 | 66.7 | 17.4 | 4.2 | 7.6 | 4.2 | 2.1 | 7.6 | 46.5 | 22.9 | 20.8 | 11.8 | 27.8 | 8.3 | 34.0 | 100.0 | 0 |
| Total | 1,935 | 49.9 | 51.4 | 32.7 | 5.2 | 4.6 | 5.2 | 12.8 | 19.1 | 43.2 | 10.3 | 9.7 | 14.1 | 31.3 | 18.6 | 42.6 | 46.9 | 53.1 |

ETS = environmental tobacco smoke.
* Refers to parent/guardian who completed the subject's baseline questionnaire.
† Reporting methods included schools that provided lists of whole grades and those that provided study subject-specific reports.

due to GI illness showed a different pattern among ethnic groups and communities from that of respiratory illnesses, with Alpine having approximately 2.5-fold higher rates than Santa Maria and Long Beach.

### Air Pollution

The patterns of $O_3$, $NO_2$, and $PM_{10}$ varied markedly within and among the communities (Figure 1). The average 10 am–6 pm ozone was highest in Riverside and lowest in Long Beach. The communities with the largest daily variations were Mira Loma, Riverside, and San Dimas, with daily levels ranging from lower than the levels observed in unpolluted regions to greater than 150 ppb.

The 24-hour average $PM_{10}$ varied by approximately the same magnitude as $O_3$; however, several of the towns with the higher $O_3$ had lower $PM_{10}$ (Figure 1). Mira Loma had the highest level and largest range in 24-hour average $PM_{10}$, and several communities had median levels below 20 $\mu g/m^3$. The 24-hour average $NO_2$ levels varied among the communities, and some communities (Lake Gregory and Lompoc) had very low levels (Figure 1). Long Beach, which had low $O_3$, had comparatively high $NO_2$. Lompoc, Santa Maria, and Atascadero had lower levels of all three of the pollutants of interest. The communities showed a large range of long-term average pollutant levels on the basis of 1995 pollution levels (Table 5). The same six communities were in the high stratum for both $NO_2$ and $PM_{10}$.

### Time-Series Regression

We found that a 30-day lag period with a cubic polynomial-constrained distributed lag model best described the data for all absences, non-illness-related absences, and respiratory absences for all three pollutant metrics of interest. A 15-day lag period provided the best fit for upper and lower respiratory absences for all three of the pollutant metrics.

### Ozone

Average $O_3$ for 10 am–6 pm was strongly associated with illness-related absences and especially respiratory absences. The summary estimates of the percentage increase in absence rates associated with $O_3$ on each of the 30 lag days are shown scaled to a 20-ppb change in $O_3$, a change that is less than the smallest range in any of the 12 communities during the 6-month period of study (Figure 2). The acute effects of $O_3$ were increased at a 3-day lag, peaked at a 5-day lag, and subsequently showed a slow decrease. Overall estimates of the effect of acute change in $O_3$ on absences are obtained by summing the area under the distributed lag curve over the 30-day lag period. Daily 1-hour peak $O_3$ produced the same overall results as analyses using the 10 am–6 pm average $O_3$.

A 20-ppb increase in $O_3$ was associated with a 62.9% absence rate increase for illness, 82.9% increase for respiratory illnesses, 45.1% increase for upper respiratory illnesses, 173.9% increase for LRI with wet cough, and

**TABLE 2. Average Daily Absence Incidence Rates per 100 Children-Days and Average Number of Children at Risk per Day on All Days and Days with Active Surveillance for Type of Absence by Selected Participant Characteristics, Air Pollution and Absence Study, January through June 1996**

| | All Days | | | Active Surveillance Days | | |
|---|---|---|---|---|---|---|
| | Absence Rate/100 | Average No. Children at Risk/Day | % | Absence Rate/100 | Average No. Children at Risk/Day | % |
| All | 3.07 | 1,502.2 | 100.0 | 3.02 | 996.4 | 100.0 |
| Sex | | | | | | |
| Females | 3.08 | 751.2 | 50.0 | 3.10 | 500.9 | 50.3 |
| Males | 3.06 | 751.0 | 50.0 | 2.93 | 495.4 | 49.7 |
| Ethnicity/race | | | | | | |
| Missing | 2.40 | 12.5 | 0.8 | 2.04 | 8.0 | 0.8 |
| White, non-Hispanic | 3.13 | 776.5 | 51.7 | 3.10 | 498.7 | 50.1 |
| Hispanic | 3.16 | 483.1 | 32.2 | 3.20 | 327.6 | 32.9 |
| Black (African-American) | 1.84 | 82.0 | 5.5 | 2.02 | 61.7 | 6.2 |
| Asian/Pacific Isle | 2.00 | 71.2 | 4.7 | 1.29 | 50.2 | 5.0 |
| Other | 3.62 | 78.1 | 5.2 | 3.89 | 51.0 | 5.1 |
| Education of signer | | | | | | |
| Missing | 3.14 | 71.2 | 4.7 | 2.97 | 45.1 | 4.5 |
| <12th grade | 3.59 | 182.5 | 12.1 | 3.73 | 124.9 | 12.5 |
| 12th grade | 3.25 | 287.2 | 19.1 | 3.19 | 189.9 | 19.1 |
| Some college/technical school | 3.16 | 651.4 | 43.4 | 3.05 | 426.9 | 42.8 |
| 4 years of college | 2.45 | 159.2 | 10.6 | 2.96 | 110.0 | 11.0 |
| Postgraduate | 2.39 | 150.8 | 10.0 | 2.35 | 99.9 | 10.0 |
| Community | | | | | | |
| Alpine | 3.23 | 158.6 | 10.6 | 3.22 | 116.0 | 11.6 |
| Lake Elsinore | 3.78 | 109.3 | 7.3 | 3.82 | 93.6 | 9.4 |
| Lake Gregory | 4.34 | 129.1 | 8.6 | 4.36 | 105.3 | 10.6 |
| Lancaster | 3.06 | 128.4 | 8.5 | 3.10 | 90.3 | 9.1 |
| Lompoc | 2.84 | 151.4 | 10.1 | 3.17 | 106.1 | 10.7 |
| Long Beach | 2.35 | 149.7 | 10.0 | 2.37 | 124.2 | 12.5 |
| Mira Loma | 3.30 | 149.5 | 10.0 | 3.35 | 143.1 | 14.4 |
| Riverside | 2.97 | 151.5 | 10.1 | 2.94 | 143.8 | 14.4 |
| San Dimas | 2.80 | 159.7 | 10.6 | 2.50 | 86.0 | 8.6 |
| Atascadero | 2.82 | 134.6 | 9.0 | 3.06 | 103.7 | 10.4 |
| Santa Maria | 2.83 | 112.9 | 7.5 | 2.57 | 83.0 | 8.3 |
| Upland | 2.29 | 143.0 | 9.5 | 2.36 | 114.6 | 11.5 |
| Diagnosed asthma | | | | | | |
| Missing | 3.15 | 45.4 | 3.0 | 3.24 | 30.5 | 3.1 |
| No | 2.98 | 1,243.3 | 82.8 | 2.94 | 827.1 | 83.0 |
| Yes | 3.65 | 213.5 | 14.2 | 3.61 | 138.7 | 13.9 |
| Reported wheeze | | | | | | |
| Missing | 2.55 | 89.6 | 6.0 | 2.73 | 61.3 | 6.2 |
| No | 2.88 | 943.2 | 62.8 | 2.81 | 630.2 | 63.2 |
| Yes | 3.55 | 469.4 | 31.2 | 3.55 | 304.9 | 30.6 |
| Any ETS | | | | | | |
| Missing | 3.17 | 49.7 | 3.3 | 3.02 | 32.8 | 3.3 |
| No | 2.93 | 1,181.0 | 78.6 | 2.86 | 786.4 | 78.9 |
| Yes | 3.67 | 271.5 | 18.1 | 3.72 | 177.2 | 17.8 |
| 7-day outdoor activities | | | | | | |
| Missing | 3.66 | 174.2 | 11.6 | 3.61 | 117.2 | 11.8 |
| ≤11.25 hours | 3.04 | 863.3 | 57.5 | 3.03 | 580.0 | 58.2 |
| >11.25 hours | 3.10 | 638.9 | 42.5 | 3.00 | 416.4 | 41.8 |
| School report method | | | | | | |
| Whole grade | 3.19 | 793.4 | 52.8 | 3.03 | 464.0 | 46.6 |
| Participants | 3.12 | 721.2 | 48.0 | 3.08 | 545.8 | 54.8 |

ETS = environmental tobacco smoke.

68.4% increase for LRI with wet cough/wheeze/asthma (Table 6). To determine the sensitivity of our estimates to the amount of smoothing used to remove seasonal variation, we refitted the models using 3 degrees of freedom and found that the estimates were essentially unchanged. For example, the effect of ozone on respiratory absences changed from an 82.9% increase to an 81.3% increase. Ozone-related increases in all absences and illness-related absences were larger in communities with lower levels of $NO_2$ or $PM_{10}$ than in communities with higher levels of $NO_2$ or $PM_{10}$ (Table 7). The acute effects of $O_3$ on respiratory illness-related absenteeism were also larger in communities with lower long-term average $PM_{10}$ (454.9%) compared with communities with high average $PM_{10}$ (42.9%).

### $PM_{10}$ AND $NO_2$

Daily 24-hour $PM_{10}$ was associated with all absences (Table 6). However, increased daily $PM_{10}$ was only associated with increases in non-illness-related absences. A change of 10 $\mu g/m^3$ in $PM_{10}$ was associated with a 22.8% increase in all types of school absences combined and with a 97.7% increase in non-illness-related ab-

**TABLE 3. Average Crude Daily Absence Incidence Rates per 100 Children-Days and Performance Characteristics of the Active Surveillance System by Selected Participant Characteristics, Air Pollution and Absence Study, January to June 1996**

| | Absence Rate/100 | | | Information Success | |
|---|---|---|---|---|---|
| | Crude Non-Illness | Crude Any Illness | Unknown Type | Mean Success Ratio | Range |
| All | 1.07 | 1.34 | 0.61 | 0.81 | 0.70–0.99 |
| Sex | | | | | |
| Females | 1.10 | 1.40 | 0.59 | 0.81 | 0.68–0.99 |
| Males | 1.05 | 1.27 | 0.61 | 0.81 | 0.65–0.99 |
| Ethnicity/race | | | | | |
| Missing | 1.25 | 0.07 | 0.73 | 0.72 | 0.57–0.93 |
| White/non-Hispanic | 1.03 | 1.42 | 0.65 | 0.82 | 0.70–0.99 |
| Hispanic | 1.15 | 1.35 | 0.70 | 0.81 | 0.57–0.99 |
| Black (African-American) | 1.05 | 0.71 | 0.26 | 0.81 | 0.59–0.93 |
| Asian/Pacific Isle | 0.39 | 0.81 | 0.10 | 0.82 | 0.67–0.94 |
| Other | 1.66 | 1.65 | 0.58 | 0.81 | 0.43–1.01 |
| Education of signer | | | | | |
| Missing | 1.01 | 1.20 | 0.76 | 0.81 | 0.56–0.96 |
| <12th grade | 1.46 | 1.37 | 0.89 | 0.80 | 0.49–0.91 |
| 12th grade | 1.08 | 1.56 | 0.55 | 0.80 | 0.44–0.92 |
| Some college/technical school | 1.09 | 1.36 | 0.60 | 0.82 | 0.69–0.99 |
| 4 years of college | 1.33 | 1.23 | 0.40 | 0.82 | 0.56–0.94 |
| Postgraduate | 0.67 | 1.20 | 0.47 | 0.81 | 0.54–0.97 |
| Community | | | | | |
| Alpine | 0.92 | 1.43 | 0.87 | 0.75 | 0.57–1.00 |
| Lake Elsinore | 1.34 | 1.80 | 0.67 | 0.84 | 0.44–1.02 |
| Lake Gregory | 1.47 | 1.83 | 1.06 | 0.76 | 0.54–0.94 |
| Lancaster | 1.14 | 1.24 | 0.73 | 0.82 | 0.67–1.02 |
| Lompoc | 0.88 | 1.74 | 0.55 | 0.83 | 0.66–0.99 |
| Long Beach | 1.16 | 0.81 | 0.40 | 0.85 | 0.75–0.97 |
| Mira Loma | 1.20 | 1.58 | 0.56 | 0.82 | 0.72–0.89 |
| Riverside | 0.87 | 1.37 | 0.69 | 0.76 | 0.55–0.90 |
| San Dimas | 0.78 | 1.19 | 0.52 | 0.82 | 0.69–0.92 |
| Atascadero | 1.01 | 1.32 | 0.72 | 0.80 | 0.30–0.96 |
| Santa Maria | 0.77 | 1.29 | 0.51 | 0.81 | 0.57–0.95 |
| Upland | 0.79 | 1.19 | 0.37 | 0.86 | 0.74–0.99 |
| Diagnosed asthma | | | | | |
| Missing | 1.44 | 1.19 | 0.61 | 0.81 | 0.58–0.95 |
| No | 1.08 | 1.26 | 0.60 | 0.81 | 0.70–0.99 |
| Yes | 1.02 | 1.88 | 0.71 | 0.81 | 0.61–0.97 |
| Reported wheeze | | | | | |
| Missing | 0.90 | 0.88 | 0.95 | 0.80 | 0.61–0.95 |
| No | 1.03 | 1.23 | 0.55 | 0.81 | 0.70–0.99 |
| Yes | 1.24 | 1.68 | 0.63 | 0.81 | 0.65–0.97 |
| Any ETS | | | | | |
| Missing | 1.37 | 0.98 | 0.68 | 0.79 | 0.44–0.94 |
| No | 1.00 | 1.28 | 0.59 | 0.81 | 0.70–0.99 |
| Yes | 1.29 | 1.79 | 0.65 | 0.81 | 0.65–0.95 |
| 7-day outdoor activities | | | | | |
| Missing | 1.32 | 1.57 | 0.71 | 0.82 | 0.62–0.99 |
| ≤11.25 hours | 1.10 | 1.35 | 0.58 | 0.81 | 0.44–0.99 |
| >11.25 hours | 1.05 | 1.36 | 0.58 | 0.81 | 0.65–0.90 |
| School report method | | | | | |
| Whole grade | 1.15 | 1.22 | 0.66 | 0.79 | 0.56–0.91 |
| Participants | 1.08 | 1.41 | 0.58 | 0.83 | 0.70–0.99 |

ETS = environmental tobacco smoke.

sences, but a 5.7% increase in illness-related absences. Daily $PM_{10}$ was not materially associated with any of the categories of respiratory illness-related absences. $NO_2$ had only a weak association with school absenteeism (Table 6).

## Discussion

We found that day-to-day changes in $O_3$ were associated with a substantial increase in school absences from both upper and lower respiratory illnesses. Absences were increased 2–3 days after exposure and reached a peak on day 5 after exposure. The short-term effects of $O_3$ on respiratory illness-related absences are consistent with a large body of evidence on the acute adverse effects of $O_3$ on children's respiratory health.[3] Exposure to $O_3$ is known to be associated with increased hospital admissions for respiratory infections among children. Hospital admission ranks as a severe outcome in the range of adverse effects, and most respiratory illnesses do not lead to hospital admission for treatment. School absences due to respiratory illnesses may usefully represent the first tier of adverse effects that are far more common than severe adverse effects.

A limited number of studies have examined the relation between $O_3$ exposure and school absenteeism. In a study in Mexico City of 111 preschool children, $O_3$ was associated with higher rates of absenteeism due to respiratory illnesses.[29] Children exposed to more than 130 ppb of $O_3$ on 2 consecutive days had a 20% increase in the occurrence of preschool-reported respiratory ill-

**TABLE 4. Type-Specific Adjusted* Absence Incidence Rates per 100 Children-Days by Selected Participant Characteristics, Air Pollution and Absence Study, January through June 1996**

| | Adjusted Non-Illness | Adjusted Any Illness | Adjusted Non-Respiratory | Adjusted Respiratory | Adjusted Upper Respiratory | Adjusted Lower Respiratory with Wet Cough | Adjusted Lower Respiratory with Wheeze | Adjusted GI Symptoms |
|---|---|---|---|---|---|---|---|---|
| All | 1.34 | 1.64 | 0.60 | 1.04 | 0.93 | 0.18 | 0.30 | 0.63 |
| Sex | | | | | | | | |
| Females | 1.36 | 1.71 | 0.62 | 1.09 | 1.00 | 0.19 | 0.30 | 0.65 |
| Males | 1.31 | 1.56 | 0.59 | 0.97 | 0.86 | 0.18 | 0.30 | 0.61 |
| Ethnicity/race | | | | | | | | |
| Missing | 1.71 | 0.10 | 0.00 | 0.10 | 0.10 | 0.00 | 0.00 | 0.00 |
| White/non-Hispanic | 1.27 | 1.73 | 0.67 | 1.06 | 0.98 | 0.21 | 0.33 | 0.75 |
| Hispanic | 1.40 | 1.65 | 0.57 | 1.08 | 0.98 | 0.19 | 0.26 | 0.57 |
| Black (African-American) | 1.35 | 0.86 | 0.10 | 0.75 | 0.68 | 0.13 | 0.47 | 0.21 |
| Asian/Pacific Isle | 0.45 | 1.00 | 0.21 | 0.79 | 0.68 | 0.10 | 0.17 | 0.14 |
| Other | 2.11 | 2.01 | 0.89 | 1.13 | 1.01 | 0.25 | 0.34 | 0.82 |
| Education of signer | | | | | | | | |
| Missing | 1.27 | 1.49 | 0.87 | 0.63 | 0.58 | 0.13 | 0.17 | 0.76 |
| <12th grade | 1.79 | 1.66 | 0.44 | 1.22 | 0.93 | 0.21 | 0.44 | 0.50 |
| 12th grade | 1.35 | 1.90 | 0.75 | 1.15 | 1.01 | 0.19 | 0.33 | 0.70 |
| Some college/technical school | 1.35 | 1.67 | 0.59 | 1.07 | 0.97 | 0.18 | 0.31 | 0.65 |
| 4 years of college | 1.76 | 1.47 | 0.37 | 1.10 | 0.99 | 0.14 | 0.38 | 0.48 |
| Postgraduate | 0.82 | 1.46 | 0.45 | 1.01 | 1.01 | 0.28 | 0.29 | 0.63 |
| Community | | | | | | | | |
| Alpine | 1.20 | 1.90 | 0.91 | 1.00 | 0.85 | 0.19 | 0.26 | 0.98 |
| Lake Elsinore | 1.67 | 2.08 | 0.76 | 1.32 | 1.17 | 0.28 | 0.56 | 0.90 |
| Lake Gregory | 1.90 | 2.28 | 0.88 | 1.41 | 1.29 | 0.30 | 0.35 | 0.88 |
| Lancaster | 1.42 | 1.47 | 0.49 | 0.98 | 0.91 | 0.12 | 0.24 | 0.64 |
| Lompoc | 1.08 | 2.09 | 0.71 | 1.38 | 1.24 | 0.24 | 0.30 | 0.73 |
| Long Beach | 1.36 | 0.96 | 0.24 | 0.72 | 0.61 | 0.21 | 0.31 | 0.35 |
| Mira Loma | 1.48 | 1.92 | 0.86 | 1.06 | 0.89 | 0.24 | 0.41 | 0.77 |
| Riverside | 1.20 | 1.82 | 0.72 | 1.09 | 1.06 | 0.20 | 0.31 | 0.85 |
| San Dimas | 0.94 | 1.44 | 0.31 | 1.13 | 0.94 | 0.16 | 0.36 | 0.38 |
| Atascadero | 1.27 | 1.61 | 0.83 | 0.78 | 0.60 | 0.11 | 0.28 | 0.66 |
| Santa Maria | 0.93 | 1.62 | 0.57 | 1.05 | 1.04 | 0.14 | 0.24 | 0.40 |
| Upland | 0.92 | 1.38 | 0.48 | 0.90 | 0.84 | 0.13 | 0.26 | 0.55 |
| Diagnosed asthma | | | | | | | | |
| Missing | 1.78 | 1.49 | 0.51 | 0.98 | 0.91 | 0.35 | 0.42 | 0.63 |
| No | 1.34 | 1.54 | 0.59 | 0.95 | 0.89 | 0.16 | 0.20 | 0.61 |
| Yes | 1.25 | 2.28 | 0.70 | 1.58 | 1.25 | 0.30 | 0.89 | 0.76 |
| Reported wheeze | | | | | | | | |
| Missing | 1.15 | 1.06 | 0.36 | 0.70 | 0.67 | 0.09 | 0.11 | 0.49 |
| No | 1.28 | 1.51 | 0.63 | 0.88 | 0.82 | 0.14 | 0.17 | 0.61 |
| Yes | 1.53 | 2.05 | 0.61 | 1.44 | 1.24 | 0.28 | 0.59 | 0.68 |
| Any ETS | | | | | | | | |
| Missing | 1.86 | 1.23 | 0.68 | 0.54 | 0.40 | 0.07 | 0.19 | 0.64 |
| No | 1.22 | 1.56 | 0.55 | 1.01 | 0.92 | 0.18 | 0.28 | 0.59 |
| Yes | 1.62 | 2.17 | 0.83 | 1.35 | 1.21 | 0.23 | 0.46 | 0.82 |
| 7-day outdoor activities | | | | | | | | |
| Missing | 1.60 | 1.93 | 0.80 | 1.14 | 1.08 | 0.21 | 0.28 | 0.79 |
| ≤11.25 hours | 1.38 | 1.65 | 0.63 | 1.03 | 0.92 | 0.18 | 0.28 | 0.63 |
| >11.25 hours | 1.30 | 1.66 | 0.58 | 1.08 | 0.97 | 0.18 | 0.34 | 0.64 |
| School report method | | | | | | | | |
| Whole grade | 1.45 | 1.55 | 0.52 | 1.03 | 0.91 | 0.20 | 0.31 | 0.64 |
| Participants | 1.33 | 1.69 | 0.61 | 1.08 | 0.98 | 0.19 | 0.32 | 0.60 |

GI = gastrointestinal; ETS = environmental tobacco smoke.
* Adjusted for interview failure using the success ratio as described in the methods section.

nesses. Studies of school absenteeism in California failed to find an association with oxidants or other pollutants, but these studies did not assess the effects of daily changes in pollutant levels on respiratory absences.[30] The relations between other air pollutants, such as $SO_2$, and school absences have also been investigated; however, the effects of $O_3$ were not examined, because levels were considered too low to have adverse effects.[31] We lack data to investigate further the reasons for the smaller effect of acute changes in $O_3$ on respiratory illness-related absences in communities with high long-term average $PM_{10}$ levels. One possible explanation is seasonal attenuation of children's responses to air pollution. Seasonal attenuation of the acute lung function response to $O_3$ exposure during high-pollution months has been reported, suggesting that long-term exposure to elevated levels of PM can affect acute response to $O_3$.[32,33]

The association of daily 24-hour average $PM_{10}$ with all absences in this study was primarily due to a relation with non-illness-related absences. The small association with illness-related absences was unexpected, because studies have shown that particulate pollution is associated with reduction in lung function, increased rates of acute bronchitis in children, increased incidence of respiratory symptoms, increased emergency room visits and hospitalizations for respiratory disease, and increased mortality.[5,17,34,35] Our study is consistent with a report by Ransom and Pope,[36] who studied the relation between school absenteeism and $PM_{10}$ in Utah Valley for 6 years between 1985 and 1990, using weekly absenteeism data

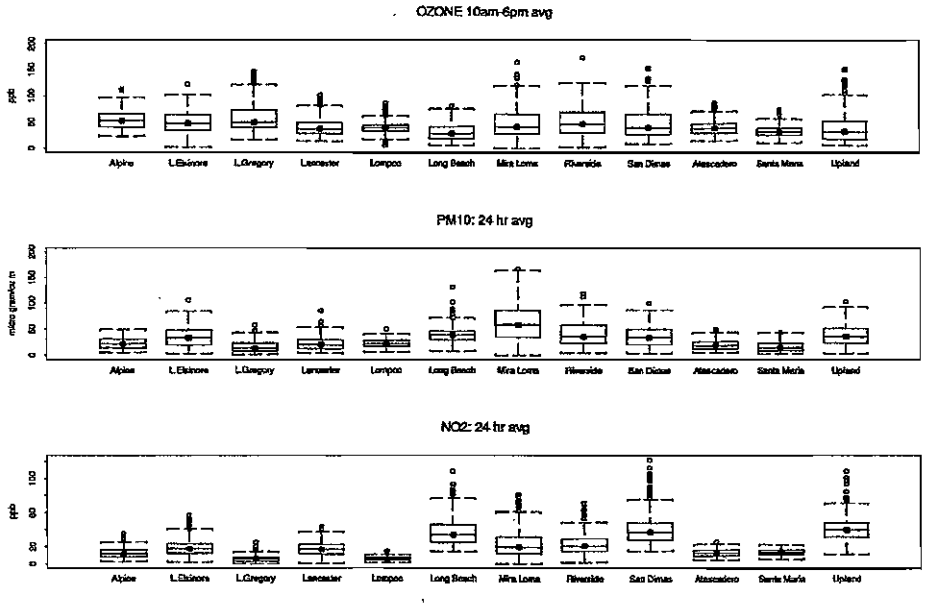


FIGURE 1. Boxplots of 10 am–6 pm average $O_3$, 24-hour average $NO_2$, and 24-hour average $PM_{10}$ in study communities (Air Pollution and Absence Study, January 1 through June 30, 1996). In the box plots, the median, first quartile, and third quartiles form the box, and the whiskers depict ±1.5 × interquartile range. Any other extreme values outside of the whiskers are plotted individually.

from one school district and daily data from one elementary school. They observed that a 100 $\mu g/m^3$ increase in the 28-day moving average of $PM_{10}$ was associated with a 40% increase in overall absences and that the effect was larger in younger children. The study did not, however, distinguish between illness and non-illness-related absenteeism. We were unable to investigate directly non-illness absences, because we did not ask about reasons for non-illness absences during interviews. We considered a number of potential sources of bias, such as incomplete control of temporal trends and the effects of temperature and differences in the effects among the communities, by conducting sensitivity analyses. We found the relations were consistent between communities and robust regardless of adjustments for temporal trends and temperature.

Acute effects of $NO_2$ on school absenteeism were not observed at the levels measured in communities during the period of study. Although $NO_2$ exposure may be associated with respiratory symptoms, little evidence exists that symptoms from $NO_2$ exposure result in school absences.[2,4,37] In a study of the relation between air pollution and absenteeism in Helsinki, Ponka[38] reported that mean weekly $NO_2$ concentrations were associated with absenteeism among adults; however, low ambient temperature accounted for the associations with absences among children in day care centers and school children.[38] In the present study, the lack of association may also reflect the narrow range of $NO_2$ exposure and possible exposure misclassification due to the use of a central site monitor to assign exposure levels. Misclassification of exposure is likely to be the same on different days within each community, suggesting that misclassification is likely to be nondifferential.[39]

In preliminary analyses, we used a bidirectional case-crossover approach to assess the air pollution and absence relation; however, the time-series analysis provides an analytic framework that efficiently uses all available information and does not have some of the conceptual drawbacks of the case-crossover approach.[40–43] The distributed lag model constrained the

**TABLE 5. Annual Average Air Pollution and Community Rankings for Ozone ($O_3$), Nitrogen Dioxide ($NO_2$), and Respirable Particles ($PM_{10}$) Based on 1995 Levels, Children's Health Study, 1995**

| Community | Annual Mean 10 am–6 pm $O_3$ (ppb) | Rank | Annual Mean Daily $NO_2$ (ppb) | Rank | Annual Mean Daily $PM_{10}$ ($\mu g/m^3$) | Rank | Stratum* ($O_3$, $PM_{10}/NO_2$) |
|---|---|---|---|---|---|---|---|
| Santa Maria | 31 | 1 | 12 | 3 | 20 | 2 | LL |
| Long Beach | 33 | 2 | 37 | 10 | 39 | 9 | LH |
| Atascadero | 43 | 3 | 13 | 4 | 22 | 4 | LL |
| Lompoc | 45 | 4 | 5 | 1 | 15 | 1 | LL |
| Lancaster | 48 | 5 | 19 | 6 | 24 | 5 | LL |
| Mira Loma | 54 | 6 | 23 | 8 | 65 | 12 | LH |
| Upland | 55 | 7 | 45 | 12 | 45 | 11 | HH |
| Lake Elsinore | 57 | 8 | 20 | 7 | 35 | 7 | HH |
| Alpine | 58 | 9 | 13 | 5 | 24 | 6 | HL |
| San Dimas | 60 | 10 | 44 | 11 | 37 | 8 | HH |
| Riverside | 62 | 11 | 25 | 9 | 44 | 10 | HH |
| Lake Gregory | 65 | 12 | 7 | 2 | 21 | 3 | HL |

* Strata were defined by ranking communities on 1995 average pollution levels and dichotomizing communities into high (H) and low (L) groups. LL = low $O_3$ and low $PM_{10}$ or $NO_2$, LH = low $O_3$ and high $PM_{10}$ or $NO_2$, HL = high $O_3$ and low $PM_{10}$ or $NO_2$, and HH = high $O_3$ and high $PM_{10}$ or $NO_2$.

**TABLE 6. Short-Term Effects of 10 am–6 pm Average Ozone ($O_3$), 24-Hour Average Respirable Particles ($PM_{10}$) and 24-Hour Average Nitrogen Dioxide ($NO_2$) on School Absence Incidence Rates [Percentage Change and 95% Confidence Limits (CL)], Air Pollution and Absence Study, January through June 1996***

| | Pollutant | | | | | |
|---|---|---|---|---|---|---|
| | $O_3$ | | $PM_{10}$ | | $NO_2$ | |
| Type of Absence | % Change | 95% CL | % Change | 95% CL | % Change | 95% CL |
| All absences | 16.3 | −2.6, 38.9 | 22.8 | 11.6, 35.2 | 3.4 | −30.6, 54.0 |
| Non-illness | 21.2 | −12.9, 69.0 | 97.7 | 72.6, 126.5 | 34.6 | −43.0, 218.2 |
| Illness | 62.9 | 18.4, 124.1 | 5.7 | −12.1, 27.0 | −4.6 | −42.4, 57.8 |
| Nonrespiratory | 37.3 | 5.7, 78.3 | 10.2 | −14.6, 42.3 | −36.8 | −69.5, 30.8 |
| Respiratory† | 82.9 | 3.9, 222.0 | −4.3 | −32.2, 35.0 | 19.6 | −36.2, 124.4 |
| URI | 45.1 | 21.3, 73.7 | 5.5 | −6.8, 19.4 | −7.4 | −30.3, 23.0 |
| LRI/wc | 173.9 | 91.3, 292.3 | −7.7 | −49.2, 67.7 | −37.5 | −73.9, 49.4 |
| LRI/W/A | 68.4 | 43.4, 97.8 | −7.1 | −34.1, 30.8 | 5.1 | −60.3, 178.0 |

URI = upper respiratory illness; LRI = lower respiratory illness; wc = wet cough; W/A = wet cough/wheeze or asthma attack.
* Results are reported for 20 ppb $O_3$, 10 $\mu g/m^3$ $PM_{10}$, and 10 ppb $NO_2$. Models are fitted using community-specific polynomial-distributed lag models (degree 3) with 30-day lag period except URI, LRI/wc†, and LRI/W/A had 15-day lag periods.
† Fifteen-day lag periods used.

acute effects of pollutants to follow a polynomial function of air pollution. Based on an objective criterion for choice of the number of lag days, minimizing the Akaike Information Criterion, a cubic polynomial that included either 15 or 30 lag days, best described the lagged effects. Other choices of the lag period length would produce consistent results for the $O_3$ effect on respiratory illness-related absences. The 15- to 30-day lag periods for the $O_3$ effects on respiratory illness-related absences are consistent with data from a number of studies showing that effects of air pollution on respiratory health outcomes may persist for up to 5 weeks.[36,44,45]

Our study enrolled and actively followed more than 2,000 4th-grade school children. The active surveillance system and modeling strategy did, however, have some limitations. Although the restriction of absences to those reported within 1 month of occurrence may have introduced bias into our study, it was adopted to minimize any recall bias of absence events by parents. On the basis of the distributions of the study population in the full and restricted sample of absence days, we found little evidence of any selection bias from the restriction. To account for the effects of incomplete ascertainment, we adjusted the denominator of the rates and the offset in the Poisson time-series models for the proportion of absences with information on absence type. To investigate the robustness of our estimates to the assumptions implicit in this adjustment, we conducted sensitivity analyses by limiting the analyses to those days with greater than 70% ascertainment. Restriction to days with nearly complete information had little effect on the magnitude of the associations. To assess further the potential for bias from the variation in ascertainment, we also examined the relations between the daily pollution and callback rates as well as absence rates and callback rates. We found that the community-specific smooth success ratios showed, in general, a weak negative correlation with ozone. Because ozone was positively correlated with absence rates over the period of study, a negative bias toward the null would be expected and cannot explain our ozone results. The correlations for $NO_2$ and $PM_{10}$ were generally smaller, making the potential for bias less likely.

We also attempted to examine variation in the relations using models stratified by asthma, ETS exposure, or other sociodemographic factors, but were unsuccessful owing to the short length of time series

**TABLE 7. Short-Term Effects of Ozone ($O_3$) [Percentage Change and 95% Confidence Limits (CL)] on School Absence Incidence Rates, Stratified by Long-Term Average 10 am–6 pm $O_3$ and 24-Hour Average Respirable Particles ($PM_{10}$) or Nitrogen Dioxide ($NO_2$),* Air Pollution and Absence Study, January through June 1996†**

| | Community Ranking | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Based on $O_3$ | | | | Based on $PM_{10}/NO_2$ | | | |
| | Low $O_3$ | | High $O_3$ | | Low $PM_{10}$ ($NO_2$) | | High $PM_{10}$ ($NO_2$) | |
| Type of Absence | % Change | 95% CL | % Change | 95% CL | % Change | 95% CL | % Change | 95% CL |
| All absences | 14.0 | −16.7, 56.1 | 16.2 | −5.8, 43.3 | 68.2 | 25.9, 124.8 | 6.4 | −7.1, 21.9 |
| Non-illness | 17.0 | −35.3, 111.9 | 20.1 | −19.2, 78.6 | 49.8 | −30.7, 223.7 | 13.6 | −20.3, 61.8 |
| Illness | 87.6 | 8.3, 225.2 | 48.8 | 3.0, 115.0 | 223.5 | 90.4, 449.7 | 38.1 | 8.5, 75.8 |
| Nonrespiratory | 29.9 | −19.8, 110.6 | 31.5 | −5.6, 83.0 | 29.6 | −32.2, 147.9 | 31.3 | −2.8, 77.4 |
| Respiratory | 136.8 | −11.5, 533.1 | 57.7 | −18.1, 203.9 | 454.9 | 90.0, 1520.0 | 42.9 | −11.2, 130.1 |

* High and low strata included the same communities for either $PM_{10}$ or $NO_2$.
† Results are reported for 20 ppb $O_3$, 10 $\mu g/m^3$ $PM_{10}$, and 10 ppb $NO_2$. Models are fitted using community-specific polynomial-distributed lag models (degree 3) with 30-day lag period.

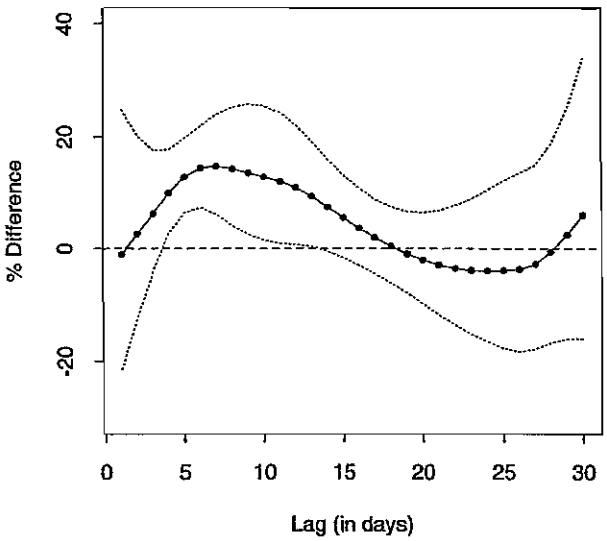


**FIGURE 2.** Distributed lag estimates and 95% confidence intervals for the effect of 10 am–6 pm $O_3$ (per 20 ppb) on respiratory illness-related absences (Air Pollution and Absence Study, January 1 through June 30, 1996).

and the low number of events within community-specific strata. Lastly, it was not feasible to examine simultaneously the acute effects of multiple pollutants using the two-stage distributed lag framework developed for this analysis. Future development of a binomial time-series model with a flexible distributed lag structure would provide the framework to include individual-level covariates and multipollutant effects in time-series analyses.

In conclusion, relatively small short-term changes in $O_3$ were associated with increases in respiratory illness-related school absences in children 9–10 years of age. Because exposures at the levels observed in this study are common, the increase in school absenteeism from respiratory illnesses associated with relatively modest day-to-day changes in $O_3$ concentration documents an important adverse impact of $O_3$ on children's health and well-being.

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# Association between Air Pollution and Lung Function Growth in Southern California Children

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**Average growth of lung function over a 4-yr period, in three cohorts of southern California children who were in the fourth, seventh, or tenth grade in 1993, was modeled as a function of average exposure to ambient air pollutants. In the fourth-grade cohort, significant deficits in growth of lung function ($FEV_1$, FVC, maximal midexpiratory flow [MMEF], and $FEF_{75}$) were associated with exposure to particles with aerodynamic diameter less than 10 μm ($PM_{10}$), $PM_{2.5}$, $PM_{10}$–$PM_{2.5}$, $NO_2$, and inorganic acid vapor ($p < 0.05$). No significant associations were observed with ozone. The estimated growth rate for children in the most polluted of the communities as compared with the least polluted was predicted to result in a cumulative reduction of 3.4% in $FEV_1$ and 5.0% in MMEF over the 4-yr study period. The estimated deficits were generally larger for children spending more time outdoors. In the seventh- and tenth-grade cohorts, the estimated pollutant effects were also negative for most lung function measures, but sample sizes were lower in these groups and none achieved statistical significance. The results suggest that significant negative effects on lung function growth in children occur at current ambient concentrations of particles, $NO_2$, and inorganic acid vapor.**

The acute health consequences of breathing polluted air are well documented, ranging from increased cardiorespiratory morbidity and mortality to increased prevalence of respiratory symptoms and decrements in lung function (1–4). Chronic health effects from exposure to air pollution have been suggested by previous studies, although whether chronic effects occur at current ambient concentrations remains uncertain (1, 2, 5–7). Children may be a particularly vulnerable population because they spend more time outdoors, are generally more active, and have higher ventilation rates than adults (8).

One approach to assessing the potential chronic effects of air pollution is to determine how pollution affects lung function growth. The broad range of air quality in southern California offers the opportunity to investigate the health effects of exposure to several pollutants, including ozone, nitrogen oxides, particles, and acids. In 1993, we initiated a 10-yr prospective study of respiratory health in children from 12 southern California communities. In this report, we examine the longitudinal lung function data from the first 4 yr of follow-up and analyze the relationship between air pollution concentrations and lung function growth.

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## METHODS

### Study Subjects

Twelve communities within a 200-mile radius of Los Angeles were selected in 1993 based on their historical air pollution levels. In each community, approximately 150 children in grade four, 75 in grade seven, and 75 in grade 10 were selected from public schools. Information concerning medical history, residential history, housing characteristics, and time spent outdoors was obtained by questionnaire. Additional characteristics of the study design have been previously described (6, 7). Spirometric evaluations of the children were conducted annually from 1993 to 1997 for the fourth- and seventh-grade cohorts, and from 1993 to 1995 for the tenth-grade cohort. A total of 3,035 children had at least two evaluations during this period. The study protocol was approved by the institutional review board for human studies at the University of Southern California, and informed written consent was provided by parents for all study subjects.

### Pulmonary Function Testing

Pulmonary function tests (PFTs) were performed at schools during the morning and early afternoon hours of spring. Each subject was asked to perform up to seven maximal forced expiratory flow–volume maneuvers using one of six rolling-seal spirometers (Spiroflow; P.K. Morgan Ltd., Gillingham, UK), from which FVC, $FEV_1$, maximal midexpiratory flow (MMEF), and forced expiratory flow rate at 75% of expired FVC ($FEF_{75}$) were recorded. A more detailed description and procedures for maneuver selection, spirometer calibration, and quality control have been previously reported (7).

### Air Pollution Data

Air pollution monitoring stations were established in each of the 12 communities as a part of the study design, with measurements for all pollutants at all sites available from 1994 onward. All stations monitored hourly concentrations of ozone ($O_3$), nitrogen dioxide ($NO_2$), and particles with aerodynamic diameter less than 10 μm ($PM_{10}$). Two-week integrated samplers were used to measure $PM_{2.5}$ and acid vapor. For statistical analysis, we computed the annual averages of the 24 h averages of $O_3$, $PM_{10}$, and $NO_2$, the annual average of 10:00 A.M. to 6:00 P.M. levels of $O_3$, the annual averages of the 2-wk averages of $PM_{2.5}$ and inorganic acid vapor ($HCl + HNO_3$), and the difference between annual average $PM_{10}$ and $PM_{2.5}$. In addition, 3-yr mean levels (1994 to 1996) in each community were computed for all pollutants.

### Statistical Analysis

Linear regression methods were used to determine whether, over the 4 yr of follow-up, average lung function growth rates of the children in each community were associated with the corresponding average pollutant levels in those communities. The outcome data consisted of 11,536 PFTs recorded from 1993 to 1997 on 3,035 study subjects in the 12 communities. Because lung function increases nonlinearly from childhood through adolescence (9), all analyses were performed separately within grade cohort (fourth, seventh, or tenth grade in 1993). A set of three regression models was used to adequately account for time, subject, and community-specific effects.

The first model was a linear regression of PFT (natural-log transformed) on age, with indicator variables for subject to obtain a separate intercept and growth slope for each child. Adjustment was made for subject- and time-specific covariates, including height (natural-log

**TABLE 1**
**CHARACTERISTICS OF THE STUDY POPULATION**

| | | No. of Subjects* | Mean No. PFTs | Female Sex (%) | Grade Cohort (%) | | | Ever Asthma (%) | Gas Stove (%) | Passive Smoke (%) | Pets (%) | Time Outdoors† (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 4th | 7th | 10th | | | | | |
| Alpine | (AL) | 252 | 3.8 | 51 | 51 | 25 | 24 | 14 | 46 | 19 | 88 | 51 |
| Atascadero | (AT) | 233 | 3.9 | 59 | 49 | 30 | 21 | 22 | 76 | 12 | 91 | 58 |
| Lake Arrowhead | (LA) | 286 | 3.9 | 52 | 52 | 27 | 21 | 14 | 86 | 19 | 86 | 48 |
| Lake Elsinore | (LE) | 258 | 3.7 | 45 | 49 | 24 | 27 | 16 | 75 | 30 | 87 | 56 |
| Lancaster | (LN) | 212 | 3.6 | 51 | 52 | 26 | 22 | 14 | 89 | 23 | 72 | 54 |
| Lompoc | (LM) | 248 | 3.6 | 50 | 39 | 27 | 34 | 12 | 82 | 18 | 78 | 60 |
| Long Beach | (LB) | 257 | 3.7 | 53 | 53 | 25 | 22 | 12 | 82 | 15 | 58 | 45 |
| Mira Loma | (ML) | 262 | 3.8 | 52 | 52 | 27 | 21 | 11 | 94 | 27 | 90 | 52 |
| Riverside | (RV) | 285 | 3.8 | 53 | 49 | 30 | 21 | 16 | 89 | 19 | 76 | 49 |
| San Dimas | (SD) | 252 | 3.9 | 53 | 47 | 27 | 26 | 18 | 90 | 21 | 74 | 52 |
| Santa Maria | (SM) | 248 | 3.6 | 52 | 48 | 26 | 26 | 14 | 85 | 18 | 55 | 49 |
| Upland | (UP) | 242 | 4.0 | 49 | 51 | 24 | 25 | 16 | 73 | 13 | 79 | 52 |
| All | | 3,035 | 3.8 | 52 | 50 | 26 | 24 | 15 | 81 | 20 | 78 | 52 |

* Number of subjects with at least 2 pulmonary function tests from 1993 to 1997.
† Percent of hours spent outdoors between 2:00 P.M. and 6:00 P.M., over 10 weekdays.

transformed), weight, body mass index, height-by-age interaction, report of asthma activity or cigarette smoking in the previous year, report of recent exercise, and interactions of each of these variables with sex. Also included as adjustment variables were room temperature and barometric pressure on the day of the test, sets of dummy variables for field technician and spirometer. Lung function growth slopes were scaled to a child with average height growth within each cohort.

The second model was a linear regression of the subject-specific adjusted growth slopes estimated from the first model on indicator variables for community, to obtain the annual average lung function growth rate in each community. Adjustment was made for subject-specific covariates, including sex, race/ethnicity (Asian, African-American, non-Hispanic white, Hispanic, other), and baseline report of doctor-diagnosed asthma. Additional variables, including report of hay fever, health insurance, regular vitamin use, and the presence in the home of mildew, pests, cockroaches, house plants, an air conditioner, or water damage were not significantly associated with any lung function growth measure at the 0.15 significance level, making them unlikely confounding variables. Because incorporation of these covariates would reduce sample sizes owing to missing values, they were excluded as adjustment variables in all models. Carpeting in the home was marginally associated with reduced MMEF ($p = 0.09$) and $FEF_{75}$ ($p = 0.09$). Models for these PFTs were estimated both with and without adjustment for carpeting, but in no case did adjustment alter an air pollution effect by more than 3% of the unadjusted estimate. For this reason, and because 7% of subjects would be excluded for missing carpet information, results described in the next section are based on the models without adjustment for this covariate. The residuals from both the first and second regression models satisfied the

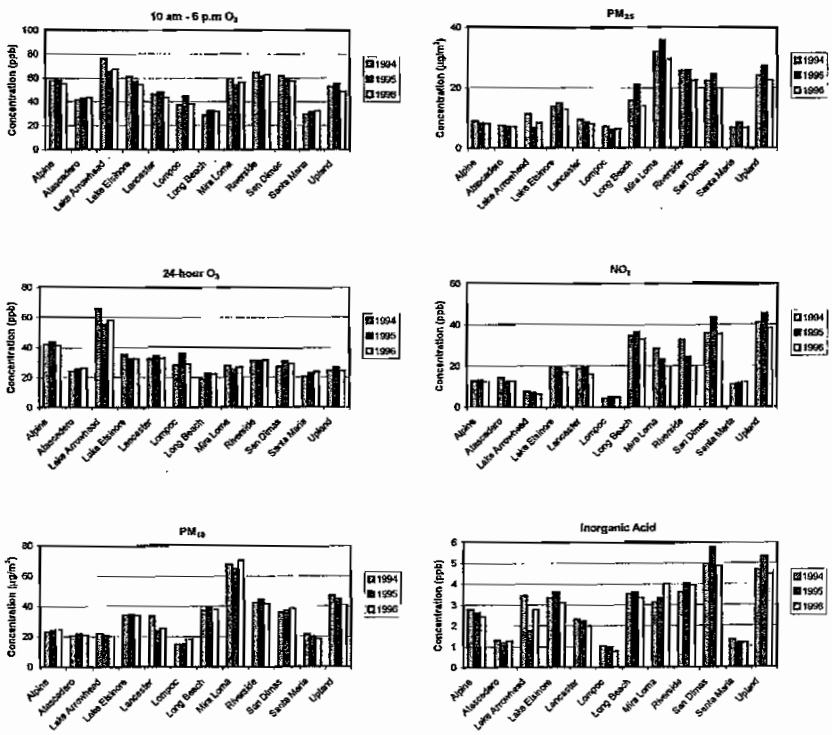


*Figure 1.* Average annual pollutant concentrations in the 12 study communities.

TABLE 2

CORRELATIONS AMONG COMMUNITY MEAN POLLUTANT LEVELS OVER THE STUDY PERIOD

| Pollutant* | $O_3$ | $PM_{10}$ | $PM_{2.5}$ | $PM_{10}$–$PM_{2.5}$ | $NO_2$ | Inorganic Acid |
|---|---|---|---|---|---|---|
| $O_3$ (10 A.M.–6 P.M.) | 0.69† | 0.28 | 0.35 | 0.15 | 0.06 | 0.50 |
| $O_3$ | — | −0.32 | −0.32 | −0.29 | −0.49 | −0.07 |
| $PM_{10}$ | — | — | 0.96‡ | 0.92‡ | 0.65§ | 0.68§ |
| $PM_{2.5}$ | — | — | — | 0.76† | 0.74§ | 0.79† |
| $PM_{10}$–$PM_{2.5}$ | — | — | — | — | 0.44 | 0.43 |
| $NO_2$ | — | — | — | — | — | 0.87‡ |

* 24-h average (unless otherwise noted) pollution level from 1994–1996.
† $p < 0.005$.
‡ $p < 0.0005$.
§ $p < 0.05$.

assumptions of normality and homoscedasticity, indicating a good fit of the linear models to the lung function data.

The 12 adjusted community-average lung growth rates from the second model were compared graphically with community mean concentrations of each pollutant, and a third linear regression was used to quantify the change in annual growth per unit increase in pollutant level. The parameter of primary interest was the slope from this third regression. These slopes were reported as the difference in estimated percent growth rate per year between the highest and lowest observed community mean levels of each pollutant, with negative differences indicating reduced growth with increased exposure. In addition to modeling the effect of each pollutant univariately, we considered all possible two-pollutant models, obtained by regressing the community-average lung growth rates on a pair of pollutants simultaneously.

For estimation and testing hypotheses, the three regression models described previously were combined into a single, linear mixed model, so that all parameters were mutually adjusted for one another and the resulting pollution effect estimates properly accounted for the different number of observations provided by each subject. The MIXED procedure in SAS (10) was utilized to fit the models, and a two-sided alternative and 0.05 significance level were used for each hypothesis test.

Additional analyses were conducted to explore the robustness of pollutant effect estimates. Models were also estimated after stratifying the data based on sex, asthma status at baseline, and time spent outdoors. The latter variable was obtained from the baseline questionnaire as the number of weekday hours spent outdoors between 2:00 P.M. and 6:00 P.M. over a 10-weekday period. Responses to this question were used to stratify subjects into either a "more outdoors" or "less outdoors" group, based on whether they fell above or below the mean of 20.8 h (52% of 40 h).

## RESULTS

The distribution of subjects with at least two PFTs during the study period is shown in Table 1. The sample included 1,498 fourth-graders in 1993, 802 seventh-graders, and 735 tenth-graders, with an average of 3.8 PFTs per child. Approximately 15% of subjects reported a history of doctor-diagnosed asthma at baseline, a proportion that varied from 11% (Mira Loma) to 22% (Atascadero) across communities. The prevalence of three indoor sources of air pollutants, passive tobacco smoke, gas stove, and the presence of pets, also varied across communities.

There was substantial variation in annual average pollutant concentrations across the 12 communities, with little year-to-year deviation in levels within each community (Figure 1). From least to most polluted community, pollutant concentrations varied by a factor of approximately 2.5 for daytime and 24-h ozone, 4 for $PM_{10}$, 5 for $PM_{2.5}$, 8 for $NO_2$, and 5 for inorganic acid. Table 2 shows correlation coefficients between community mean pollutant levels over the study period. Four of the pollutants ($PM_{10}$, $PM_{2.5}$, $NO_2$, and inorganic acid) were

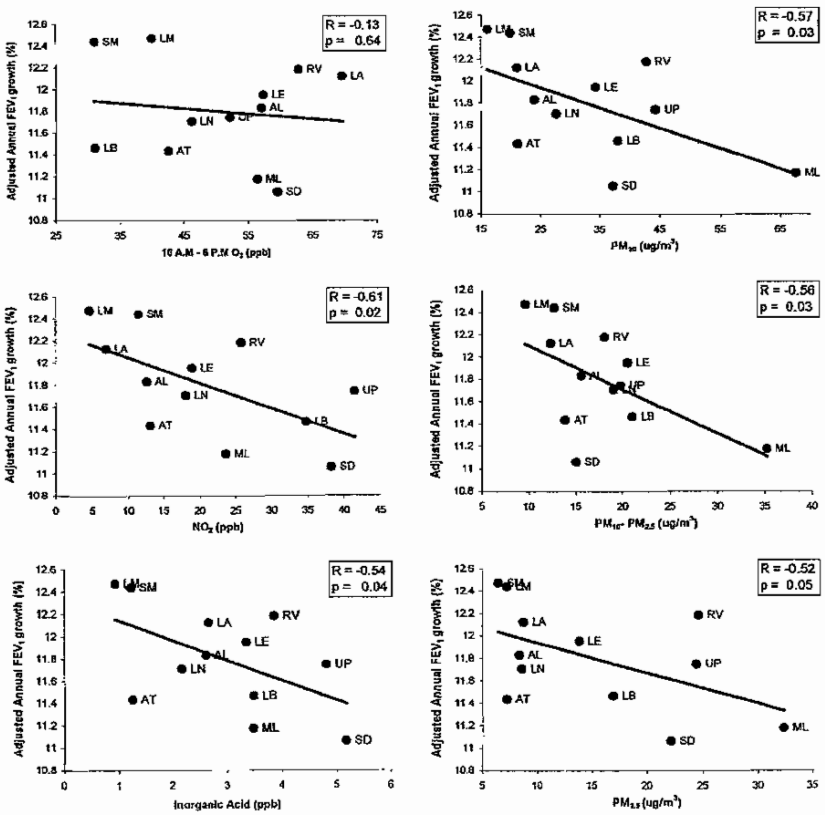


*Figure 2.* Adjusted average annual $FEV_1$ growth rates for the fourth-grade cohort in the 12 communities versus the mean pollutant levels over the study period. The two-letter abbreviations for each community are shown in Table 1.

TABLE 3

DIFFERENCE IN ANNUAL PERCENT GROWTH RATES FROM THE LEAST TO MOST POLLUTED COMMUNITY, BY GRADE COHORT

| | | 4th Grade | | 7th Grade | | 10th Grade | |
|---|---|---|---|---|---|---|---|
| | | Difference in Growth* | | Difference in Growth* | | Difference in Growth* | |
| Pollutant | PFT | % | (95% CI) | % | (95% CI) | % | (95% CI) |
| $O_3$ (10–6) | FVC | −0.22 | (−0.79, 0.36) | −0.10 | (−0.68, 0.47) | 0.11 | (−0.84, 1.07) |
| | $FEV_1$ | −0.19 | (−0.99, 0.62) | 0.20 | (−0.41, 0.81) | 0.24 | (−1.03, 1.54) |
| | MMEF | −0.24 | (−1.41, 0.95) | −0.37 | (−2.20, 1.50) | 0.29 | (−3.50, 4.23) |
| | $FEF_{75}$ | −0.85 | (−2.38, 0.70) | −0.31 | (−1.95, 1.35) | 0.49 | (−3.36, 4.49) |
| $O_3$ | FVC | 0.17 | (−0.79, 1.15) | 0.39 | (−0.51, 1.29) | 0.03 | (−1.57, 1.65) |
| | $FEV_1$ | 0.56 | (−0.73, 1.87) | 0.83 | (−0.12, 1.79) | 0.79 | (−1.33, 2.95) |
| | MMEF | 0.96 | (−0.84, 2.79) | 0.51 | (−2.45, 3.56) | 0.35 | (−5.94, 7.07) |
| | $FEF_{75}$ | 0.69 | (−1.88, 3.32) | 0.38 | (−2.13, 2.95) | 1.08 | (−5.34, 7.92) |
| $PM_{10}$ | FVC | −0.58 | (−1.14, −0.02)† | −0.45 | (−1.03, 0.13) | 0.07 | (−0.99, 1.13) |
| | $FEV_1$ | −0.85 | (−1.59, −0.10)† | −0.44 | (−1.10, 0.23) | −0.46 | (−1.84, 0.94) |
| | MMEF | −1.32 | (−2.43, −0.20)† | −0.48 | (−2.51, 1.59) | −0.71 | (−4.87, 3.63) |
| | $FEF_{75}$ | −1.63 | (−3.14, −0.11)† | −0.50 | (−2.26, 1.29) | −1.54 | (−5.61, 2.71) |
| $PM_{2.5}$ | FVC | −0.47 | (−0.94, 0.01) | −0.42 | (−0.89, 0.05) | 0.19 | (−0.68, 1.07) |
| | $FEV_1$ | −0.64 | (−1.28, 0.01) | −0.32 | (−0.88, 0.24) | −0.25 | (−1.41, 0.93) |
| | MMEF | −1.03 | (−1.95, −0.09)† | −0.29 | (−1.99, 1.44) | −0.17 | (−3.66, 3.46) |
| | $FEF_{75}$ | −1.31 | (−2.57, −0.03)† | −0.26 | (−1.75, 1.25) | −0.79 | (−4.27, 2.82) |
| $PM_{10}$–$PM_{2.5}$ | FVC | −0.57 | (−1.20, 0.06) | −0.35 | (−1.02, 0.31) | −0.17 | (−1.32, 0.99) |
| | $FEV_1$ | −0.90 | (−1.71, −0.09)† | −0.49 | (−1.21, 0.24) | −0.68 | (−2.15, 0.81) |
| | MMEF | −1.37 | (−2.57, −0.15)† | −0.64 | (−2.83, 1.60) | −1.41 | (−5.85, 3.25) |
| | $FEF_{75}$ | −1.62 | (−3.24, 0.04) | −0.74 | (−2.65, 1.20) | −2.32 | (−6.60, 2.17) |
| $NO_2$ | FVC | −0.53 | (−1.01, −0.05)† | −0.43 | (−0.93, 0.07) | −0.23 | (−1.13, 0.68) |
| | $FEV_1$ | −0.77 | (−1.41, −0.13)† | −0.41 | (−1.00, 0.17) | −0.75 | (−1.89, 0.41) |
| | MMEF | −1.08 | (−2.07, −0.08)† | −0.30 | (−2.07, 1.49) | −1.13 | (−4.68, 2.56) |
| | $FEF_{75}$ | −1.37 | (−2.71, −0.01)† | −0.32 | (−1.88, 1.26) | −1.28 | (−4.87, 2.44) |
| Acid | FVC | −0.57 | (−1.06, −0.07)† | −0.39 | (−0.93, 0.15) | −0.23 | (−1.15, 0.70) |
| | $FEV_1$ | −0.73 | (−1.42, −0.03)† | −0.18 | (−0.81, 0.44) | −0.65 | (−1.84, 0.56) |
| | MMEF | −1.03 | (−2.09, 0.05) | −0.30 | (−2.14, 1.57) | −1.31 | (−4.93, 2.44) |
| | $FEF_{75}$ | −1.47 | (−2.87, −0.05)† | −0.35 | (−1.99, 1.32) | −1.11 | (−4.80, 2.71) |

* Community-average growth rates were adjusted for the covariates listed in METHODS. Differences in annual percent growth rate are shown per increase in annual average of 38.6 ppb of $O_3$ (10:00 A.M.–6:00 P.M.), 55 ppb of $O_3$, 51.5 μg/m³ of $PM_{10}$, 25.9 μg/m³ of $PM_{2.5}$, 25.6 μg/m³ of $PM_{10}$–$PM_{2.5}$, 36.8 ppb of $NO_2$, and 4.3 ppb of inorganic acid vapor.

† $p < 0.05$.

strongly correlated with one another. Coarse thoracic particle level ($PM_{10}$–$PM_{2.5}$) was significantly correlated with $PM_{10}$ ($r = 0.92$) and $PM_{2.5}$ ($r = 0.76$), but not with any other pollutant. The two $O_3$ metrics were significantly correlated with each other ($r = 0.69$), but not with any of the remaining pollutants.

In the fourth-grade cohort, $FEV_1$ increased at an average rate of 11.8% per year during the study period, with comparable growth rates in males (11.7%) and females (11.9%). The average annual $FEV_1$ growth rates were lower in the seventh-grade (8.0%) and tenth-grade (1.7%) cohorts. In both the seventh- and tenth-grade cohorts, average growth rates for boys (12.3% and 3.3%, respectively) were higher than for girls (4.6% and 0.4%, respectively). The magnitudes and patterns of cohort- and sex-specific growth rates were similar for the other PFTs.

For the fourth-grade cohort, Figure 2 shows the adjusted mean $FEV_1$ growth rates in each community, plotted against the corresponding mean concentrations of $PM_{10}$, $PM_{2.5}$, $PM_{10}$–$PM_{2.5}$, $O_3$, $NO_2$, and inorganic acid vapor, with the fitted regression line and correlation coefficient. Across the 12 communities, $FEV_1$ growth rates ranged from 11.1% (San Dimas) to 12.5% (Lompoc). From the lowest to highest observed concentrations of each pollutant, the predicted differences in annual growth rate were −0.85% for $PM_{10}$ ($p = 0.026$), −0.64% for $PM_{2.5}$ ($p = 0.052$), −0.90% for $PM_{10}$–$PM_{2.5}$ ($p = 0.030$), −0.77% for $NO_2$ ($p = 0.019$), and −0.73% for inorganic acid vapor ($p = 0.042$). The slope with 10:00 A.M.–6:00 P.M. average $O_3$ was negative but nonsignificant. Approximately 35% of the variance in adjusted community-average growth rates was explained by either $PM_{10}$ or $NO_2$ concentrations. For $PM_{10}$ and $PM_{10}$–$PM_{2.5}$, the high concentrations in Mira Loma gave this community a large potential influence on the effect estimates. However, elimination of this community from the analysis resulted in slightly larger effect estimates for both $PM_{10}$ (−0.9%) and $PM_{10}$–$PM_{2.5}$ (−1.2%), although the statistical significance for each was reduced ($p = 0.19$ and $p = 0.18$, respectively) owing to the reduced sample size and range of exposure.

Table 3 shows the corresponding differences in growth rate for all the PFTs in the fourth-, seventh-, and tenth-grade cohorts. In the fourth-grade cohort, significant associations were observed between lung function growth and $PM_{10}$, $PM_{2.5}$, $PM_{10}$–$PM_{2.5}$, $NO_2$, and inorganic acid, with the largest deficits observed for the flow rate measures (MMEF and $FEF_{75}$). Neither metric of ozone was significantly associated with growth in any of the PFTs. In the seventh- and tenth-grade cohorts, almost all effect estimates for $PM_{10}$, $PM_{2.5}$, $PM_{10}$–$PM_{2.5}$, $NO_2$, and inorganic acid vapor were negative, but the confidence intervals were wide and none of them achieved statistical significance.

The associations observed in the fourth-grade cohort remained significant in a variety of sensitivity analyses. Table 4

TABLE 4

DIFFERENCE IN ANNUAL $FEV_1$ PERCENT GROWTH RATES FROM THE LEAST TO MOST POLLUTED COMMUNITY FOR $PM_{10}$ AND $NO_2$, FOURTH GRADE COHORT, FROM A VARIETY OF MODELS

| | Ambient $PM_{10}$ | | Ambient $NO_2$ | |
|---|---|---|---|---|
| | Difference in Growth* | | Difference in Growth* | |
| Model | % | (95% CI) | % | (95% CI) |
| 1. Main model† | −0.85 | (−1.59, −0.10)‡ | −0.77 | (−1.41, −0.13)‡ |
| 2. 1 + gas stove | −0.88 | (−1.63, −0.13)‡ | −0.79 | (−1.43, −0.15)‡ |
| 3. 1 + passive smoke | −0.94 | (−1.71, −0.17)‡ | −0.83 | (−1.50, −0.16)‡ |
| 4. 1 + pets | −0.80 | (−1.52, −0.08)‡ | −0.76 | (−1.36, −0.15)‡ |
| 5. 1, nonasthmatics only | −0.82 | (−1.48, −0.15)‡ | −0.68 | (−1.30, −0.05)‡ |
| 6. 1, asthmatics only | −0.75 | (−2.84, 1.38) | −1.39 | (−2.96, 0.20) |

* *See* footnote to Table 3.
† Equivalent to the results for $FEV_1$ in fourth graders shown in Table 3.
‡ $p < 0.05$.

shows effect estimates for $PM_{10}$ and $NO_2$ on $FEV_1$ from several models, with the corresponding estimates from Table 3 included for comparison (Model 1). Adjustment for gas stove (Model 2), passive smoke (Model 3), or pets (Model 4) resulted in little change in effect estimates or statistical significance. The associations also remained significant in the subset of nonasthmatic children (Model 5). In asthmatic children (Model 6), although the effect estimates were as large for $PM_{10}$ and larger for $NO_2$, the sample size was small (n = 207) and neither association achieved statistical significance. Analogous sensitivity modeling of the other PFTs produced results similar to those shown for $FEV_1$.

In two-pollutant models for $FEV_1$, adjustment for community mean concentration of 10:00 A.M.–6:00 P.M. $O_3$ had little impact on the effect estimates or significance levels of any other pollutant (Table 5, column 1). The $O_3$ effect estimates with adjustment for any other pollutant were all close to zero and nonsignificant (Table 5, row 1). In a two-pollutant particle model, both the $PM_{2.5}$ and $PM_{10}$–$PM_{2.5}$ effect estimates were negative (−0.54 and −0.63, respectively), but each was lower than its corresponding univariate estimate (−0.64 and −0.90, respectively). This reduction of the particle effect estimates in the two-pollutant model is expected given the positive correlation between these pollutants (Table 2). Similarly, the effect estimates for other two-pollutant combinations are less than their corresponding univariate estimates, although in almost all cases they retain their negative sign.

TABLE 5

DIFFERENCE IN ANNUAL $FEV_1$ PERCENT GROWTH RATES FROM THE LEAST TO THE MOST POLLUTED COMMUNITY, FOURTH-GRADE COHORT, TWO-POLLUTANT MODELS

| Main | Adjustment Pollutant | | | | | |
|---|---|---|---|---|---|---|
| Pollutant* | $O_3$ (10–6) | $PM_{10}$ | $PM_{2.5}$ | $PM_{10}$–$PM_{2.5}$ | $NO_2$ | Acid |
| 1. $O_3$ (10–6) | **−0.19** | 0.03 | 0.06 | −0.08 | 0.15 | 0.24 |
| 2. $PM_{10}$ | −0.86† | **−0.85**† | −1.27 | −0.54 | −0.48 | −0.56 |
| 3. $PM_{2.5}$ | −0.67‡ | 0.37 | **−0.64**‡ | −0.54 | −0.45 | −0.61 |
| 4. $PM_{10}$–$PM_{2.5}$ | −0.89† | −0.37 | −0.63 | **−0.90**† | −0.61 | −0.65 |
| 5. $NO_2$ | −0.76† | −0.50 | −0.60 | −0.56 | **−0.77**† | −0.65 |
| 6. Acid | −0.86† | −0.39 | −0.47 | −0.50 | −0.14 | **−0.73**† |

* Each row gives effect estimates for the indicated pollutant, after adjustment for the pollutant listed at the top of the column. Boldface estimates are from the single-pollutant models shown in Table 3. *See* Table 3, footnote *, for a description of units.
† $p < 0.05$.
‡ $p < 0.10$.

The magnitude of air pollutant effects in the fourth-grade cohort was greater in those who spent more time outdoors than in those who spent more time indoors (Table 6). For example, the difference in annual $FEF_{75}$ growth rate from highest to lowest $NO_2$ concentrations was −2.49% (p = 0.02) in more-outdoors children, but only −1.12% (p = 0.35) in less-outdoors children. There were no clear trends in the relationships between lung function growth and ozone as they related to time spent outdoors. In a separate analysis, stratification by sex in the fourth-grade cohort revealed negative effect estimates for particulates, $NO_2$, and inorganic acid vapor in both males and females (data not shown), with no significant difference in effect between the sexes.

Based on the estimated adjusted annual growth rates in the fourth-grade cohort, Table 7 shows estimates of the cumulative deficit in lung function caused by 4 yr of air pollution exposure. Predicted lung function in 1997 for a child exposed to the highest observed concentrations of $PM_{10}$ or $NO_2$ since 1993 were between 93.9% and 97.9% of those predicted for the same child exposed to the lowest observed concentrations. The flow rates (MMEF and $FEF_{75}$) showed larger deficits in predicted lung function than the volume measures (FVC and $FEV_1$).

TABLE 6

DIFFERENCE IN ANNUAL PERCENT GROWTH RATES FROM LEAST TO MOST POLLUTED COMMUNITY FOR CHILDREN IN THE FOURTH-GRADE COHORT, STRATIFIED BY TIME OUTDOORS

| | | More Outdoors* (*n* = 532) | | Less Outdoors* (*n* = 642) | |
|---|---|---|---|---|---|
| | | Difference in Growth† | | Difference in Growth† | |
| Pollutant | PFT | % | (95% CI) | % | (95% CI) |
| $O_3$ (10–6) | FVC | 0.12 | (−0.54, 0.78) | −0.05 | (−0.63, 0.53) |
| | $FEV_1$ | −0.11 | (−1.19, 0.99) | −0.10 | (−0.79, 0.60) |
| | MMEF | −0.46 | (−2.52, 1.64) | 0.16 | (−1.34, 1.69) |
| | $FEF_{75}$ | −0.41 | (−2.73, 1.98) | −0.76 | (−3.15, 1.69) |
| $O_3$ | FVC | 0.41 | (−0.60, 1.43) | 0.23 | (−0.68, 1.14) |
| | $FEV_1$ | 0.91 | (−0.64, 2.47) | 0.76 | (−0.35, 1.87) |
| | MMEF | 1.50 | (−1.40, 4.48) | 2.16 | (−0.26, 4.64) |
| | $FEF_{75}$ | 1.81 | (−1.72, 5.47) | 1.78 | (−1.97, 5.68) |
| $PM_{10}$ | FVC | −0.24 | (−0.91, 0.45) | −0.60 | (−1.22, 0.01) |
| | $FEV_1$ | −0.87 | (−1.86, 0.14) | −0.81 | (−1.57, −0.03)‡ |
| | MMEF | −1.88 | (−3.55, −0.17)‡ | −1.20 | (−2.86, 0.49) |
| | $FEF_{75}$ | −2.34 | (−4.65, 0.03) | −0.88 | (−3.53, 1.83) |
| $PM_{2.5}$ | FVC | −0.17 | (−0.74, 0.40) | −0.45 | (−0.97, 0.07) |
| | $FEV_1$ | −0.67 | (−1.53, 0.21) | −0.68 | (−1.32, −0.03)‡ |
| | MMEF | −1.56 | (−3.00, −0.10)‡ | −1.09 | (−2.49, 0.33) |
| | $FEF_{75}$ | −1.92 | (−3.88, 0.08) | −1.15 | (−3.26, 1.01) |
| $PM_{10}$–$PM_{2.5}$ | FVC | −0.27 | (−1.00, 0.46) | −0.65 | (−1.31, 0.01) |
| | $FEV_1$ | −0.93 | (−1.98, 0.14) | −0.75 | (−1.57, 0.07) |
| | MMEF | −1.83 | (−3.73, 0.10) | −0.98 | (−2.76, 0.83) |
| | $FEF_{75}$ | −2.29 | (−4.78, 0.27) | −0.15 | (−3.13, 2.91) |
| $NO_2$ | FVC | −0.41 | (−1.02, 0.20) | −0.30 | (−0.87, 0.28) |
| | $FEV_1$ | −1.00 | (−1.79, −0.21)‡ | −0.57 | (−1.29, 0.15) |
| | MMEF | −1.90 | (−3.39, −0.39)‡ | −1.13 | (−2.68, 0.44) |
| | $FEF_{75}$ | −2.49 | (−4.57, −0.36)‡ | −1.12 | (−3.43, 1.25) |
| Acid | FVC | −0.33 | (−0.97, 0.32) | −0.32 | (−0.94, 0.30) |
| | $FEV_1$ | −0.93 | (−1.87, 0.01) | −0.55 | (−1.31, 0.23) |
| | MMEF | −1.88 | (−3.58, −0.14)‡ | −0.89 | (−2.55, 0.80) |
| | $FEF_{75}$ | −2.34 | (−4.55, −0.08)‡ | −1.13 | (−3.60, 1.41) |

* More (less) outdoors includes subjects who reported being outdoors more than (less than) 52% of the hours between 2:00 P.M. and 6:00 P.M. over a 10-d period.
† *See* footnote to Table 3.
‡ $p < 0.05$.

TABLE 7

PREDICTED LUNG FUNCTION IN 1997 FOR A CHILD IN THE FOURTH-GRADE COHORT EXPOSED TO 4-yr OF EITHER LOW OR HIGH POLLUTION LEVELS

| | FVC (ml) | $FEV_1$ (ml) | MMEF (ml/s) | $FEF_{75}$ (ml/s) |
|---|---|---|---|---|
| Mean in 1993 | 2,365 | 2,048 | 2,366 | 1,479 |
| Predicted in 1997* | | | | |
| Lowest pollution | 3,713 | 3,238 | 3,695 | 2,403 |
| Highest $PM_{10}$ | 3,622 (97.5%)† | 3,127 (96.6%) | 3,511 (95.0%) | 2,257 (93.9%) |
| Highest $NO_2$ | 3,637 (97.9%) | 3,145 (97.1%) | 3,549 (96.0%) | 2,284 (95.0%) |

* Predicted lung function was obtained by applying the estimated adjusted annual growth rates in the least and most polluted communities to the 1993 values. For example, rates used for $FEV_1$ are based on the regression line shown in Figure 2. Lowest pollution corresponds to levels in Lompoc, with average $PM_{10}$ = 16.1 μg/m³ and $NO_2$ = 4.6 ppb, while highest $PM_{10}$ = 67.6 μg/m³ (Mira Loma) and highest $NO_2$ = 41.4 ppb (Upland).

† Percent of the predicted value for lowest pollution exposure.

## DISCUSSION

In our fourth-grade cohort of southern California children, exposure to ambient particles, $NO_2$, or inorganic acid vapor was associated with reduced lung function growth. Negative pollution effect estimates were observed in both asthmatic and healthy children. In contrast to our previous cross-sectional findings (7), where pollutant effects on lung function level were observed primarily in females, we found no significant difference between the sexes in the relationship between lung function growth and air pollution. Over the 4 yr of follow-up, children exposed to the highest observed concentrations of $PM_{10}$ were estimated to experience a cumulative deficit of 3.4% in $FEV_1$ and 6.1% in $FEF_{75}$, relative to children exposed to the lowest observed levels. This indicates that pollutants may impair both large and small airway function, although there were larger estimated deficits observed in measures of small airway damage (MMEF and $FEF_{75}$). In the seventh- and tenth-grade cohorts, confidence intervals on the pollutant effect estimates were wide owing to the smaller sample sizes in these groups, and none of the associations was statistically significant at the 5% level. However, the pollutant effect estimates were negative in both the seventh- and tenth-grade cohorts, indicating that the deficits observed for children in the fourth-grade cohort are not likely to be reversed as they age through adolescence.

As in any epidemiologic study, it is possible that the observed results are the result of underlying associations of both the outcome and exposure to some confounding variable. In our study, several potential confounders were considered, including personal and housing characteristics and indoor sources of air pollutants, but none explained the observed associations between ambient air pollution and lung function growth. Additional analysis showed that neither air pollution concentrations on the day before to the PFT nor acute respiratory illness on the day of the PFT were confounders. Another potential source of bias in a cohort study is differential loss to follow-up with respect to both exposure and outcome. This could occur, for example, if a child in a polluted community moved away because air pollution was adversely affecting his or her respiratory health. However, baseline lung function levels and community mean ambient pollutant exposure were not significantly different between subjects who left the study within 2 yr of entry compared with those who remained on study, making this an unlikely source of bias.

Ambient air pollution was associated with larger estimated deficits in lung function growth, particularly for MMEF and $FEF_{75}$, in children who spent more time outdoors than in children who spent more time indoors. Provided exposures are higher in children spending more time outdoors than indoors, this finding is consistent with a detrimental effect of ambient pollutants on lung function growth. The indoor/outdoor (I/O) ratio, i.e., the amount of outdoor air pollutant that penetrates indoors, has an upper bound of 1.0 (complete penetration) and a lower bound of 0.0 (no penetration). Interestingly, the pollutants with lower I/O ratios (e.g., $PM_{10}$–$PM_{2.5}$, $NO_2$) show larger discrepancies in effect estimates between more- and less-outdoor children than $PM_{2.5}$, which has a high I/O ratio. This pattern is what one would expect if exposure to one or more of these ambient pollutants is having an adverse effect. Although indoor concentrations of ozone are known to be much lower than outdoor levels, there were no apparent trends in ozone effect estimates with respect to time spent outdoors.

In southern California, motor vehicle emissions, in conjunction with various photochemical reactions, are a major source of ambient particles, $NO_2$, and inorganic acid (primarily nitric). Due to the high correlation in concentrations across communities, we were unable to identify the independent effects of each pollutant, although our two-pollutant models do suggest that no single pollutant that we measured is responsible for the observed deficits in lung function growth. There may also be an air pollutant we did not specifically measure (e.g., diesel exhaust particles) that is correlated with those we did and that is primarily responsible for the observed health effects. Associations between lung function and mixtures of air pollutants have also been previously demonstrated (7, 11–14).

In prior studies, particulate matter has been associated with chronic respiratory symptoms (15–18) and recently with lung function growth in children (19), although previously reported associations with lung function have been inconsistent (15–17). Particle strong acidity, characterized by sulfur dioxide–derived acidic sulfate particles, has been associated with bronchitis (17) and lung function (20). It is unlikely that this pollutant is responsible for our observed effects, because ambient air during the 1990s in southern California had low concentrations of $SO_2$ and acidic sulfate particles. As in most regions, fine and coarse particle concentrations in the Los Angeles air basin arise from different sources (21). The primary sources that contribute to fine particle concentrations are diesel engine exhaust, food cooking operations, wood burning, and fine diameter paved and unpaved road and crustal dust (22). Emissions from gasoline power engines and other combustion sources make smaller contributions. Primary sources for coarse particle concentration are paved and unpaved road dust and crustal material, which accounts for 45% of the $PM_{10}$ mass concentration, and transformed sea-salt particles that are formed over the ocean and transported to the basin by prevailing winds. These sources produce a background aerosol that further interacts with gas-phase combustion emissions whose chemical characteristics evolve during atmospheric reactions to produce particulate-phase ammonium nitrate, ammonium sulfate, and secondary organic carbon compounds. The gas-to-particle conversion processes continue as the aerosol ages and moves downwind resulting in increases in concentration and composition changes of particles until fine particle mass is primarily composed of secondary reaction products.

The emission sources and atmospheric processes that produce particulates have implication for the interpretation of our data. Because the processes are coupled, characteristics of

the atmospheric aerosol are spatially and temporally correlated. Areas with the highest mass concentration of $PM_{10}$ and $PM_{2.5}$ also have the highest secondary aerosol concentrations (ammonium nitrate, ammonium sulfate) and the gas phase with the greatest age from time of emission. It follows that any chronic respiratory effects associated with particulate mass concentration might be explained by particle primary sources or by particle composition or concentrations of other pollutants that are positively correlated with the age of the aerosol. Our current exposure data do not permit us to discriminate among these possibilities.

Unlike other atmospheric pollutants, the effect of $NO_2$ has been examined in epidemiologic studies relatively unconfounded by multiple pollutant mixes, because $NO_2$ is common in indoor air contaminated by emissions from pilot lights and gas stoves at concentrations that may approach outdoor levels. Animal studies suggesting that $NO_2$ may enhance the infectivity of respiratory pathogens have resulted in extensive study of the effects of gas stoves on illness and lung function (2). In one of the few prospective studies in humans, Dutch children were followed over a 2-yr period with serial lung function measurements, but there was no consistent relationship between growth of lung function and a single measurement of indoor $NO_2$ (23). In early analyses of data from the Six Cities studies, lower levels of $FEV_1$ and FVC were observed in children living in homes with gas stoves (24, 25), but in subsequent analysis there was no evidence that lung function growth was correlated with gas stove exposure (26). In a subsample of children from the Six Cities study for whom indoor $NO_2$ was measured, there was no consistent effect of measured $NO_2$ on lung function level in spite of a relatively strong association between respiratory symptoms and $NO_2$ (27). Other studies of the effect of indoor sources of $NO_2$ on lung function in children have also not been consistent (2).

The high ambient concentration of $NO_2$ is the primary source of gaseous nitric acid present in southern California air. Although there has been little previous epidemiologic study of nitric acid, exposure to 50 parts per billion (ppb) in chamber studies has been shown to result in modest acute reductions in $FEV_1$ among children with asthma (28). In an epidemiologic study of Dutch children, modest acute deficits in flow rates were associated with same-day exposure to low levels of ambient nitrous acid (29), a gaseous acid that exists in equilibrium with nitric acid. In a large cross-sectional study of children in 24 North American cities, decrements in FVC and $FEV_1$ were associated with chronic exposure to strong acid sulfate aerosols after adjustment for ozone exposure (20). Experimental and toxicologic studies of acid sulfate aerosols suggest that the irritant potential is related to the $H^+$ concentration, especially in association with metal ions (1). However, it is not clear that the effects of gaseous nitric acid are the same as for acid sulfate aerosols, even if $H^+$ is responsible for lung damage. Gaseous nitric acid may be buffered differently by oral ammonia, or variations in deposition by particle size for sulfate aerosols may result in respiratory effects that differ from those of nitric acid.

In a recent longitudinal study of children in Austria, Frischer and coworkers concluded that exposure to ambient ozone was associated with reduced lung function growth (30), although they also observed significant associations with $NO_2$, $SO_2$, and $PM_{10}$. Some additional epidemiologic studies have also suggested that chronic exposure to ozone has long-term effects on lung function (31, 32), findings that have some support from animal studies (1). However, interpretation of the existing epidemiologic evidence is hampered by inability to separate the effects of other copollutants from the effects of ozone (33). The present study was originally designed to assess the independent effects of ozone by minimizing its correlation with other copollutants, and, as expected, observed long-term average ozone concentrations were not significantly correlated with the other pollutants (Table 2). In light of this, our results provide little support for a substantial long-term effect of ozone on lung function growth in children. This could potentially be explained by misclassification of exposure from using central monitor pollutant levels or by low sensitivity of spirometry to detect small airway effects. However, we observed consistent effects for other pollutants using the same exposure estimation methodology, indicating that the lack of an observed ozone effect is unlikely to be the result of these factors. As shown in Figure 1, the variation across communities in mean ozone concentrations (approximately twofold from least to most polluted) was less than for the other pollutants. This modest range in ozone exposure, in conjunction with the low I/O ratio of ambient ozone, may also explain why we did not observe a significant ozone association.

In summary, we obtained annual lung function measures on a cohort of 3,035 school-aged children over a 4-yr period. After appropriate adjustment for personal and household characteristics, ambient air pollution was correlated with statistically significant, and perhaps physiologically important, decreases in lung function growth. The estimated deficit in annual $FEV_1$ growth rate of 0.9% per year across the range of $PM_{10}$ exposure exceeds the 0.2% annual decrement that has been reported for passive smoke exposure in children (26). The results suggest that exposure to air pollution may lead to a reduction in maximal attained lung function, which occurs early in adult life, and ultimately to increased risk of chronic respiratory illness in adulthood. Data from the remainder of our study will help to elucidate the relationships between respiratory health and long-term exposure to ambient air pollutants, while additional follow-up of the cohort beyond graduation will be necessary to determine whether the observed air pollution–associated deficits in lung function have an impact on adult respiratory health.

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Merced/Mariposa County Asthma Coalition


# Report to the Community on Asthma

The Merced/Mariposa County Asthma Coalition (MMCAC) is a community-based health organization whose mission is: Controlling asthma through awareness and education. The coalition was formed in 1997, and since then has grown into a diverse body consisting of over 120 volunteer members.

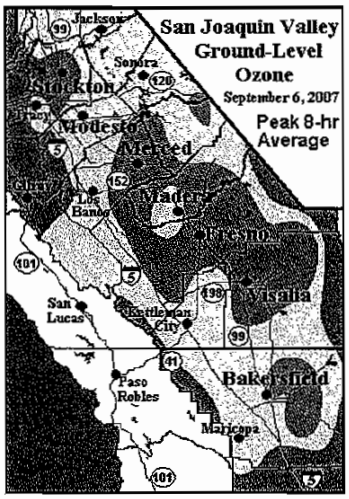
## CONTROLLING ASTHMA THROUGH AWARENESS AND EDUCATION.

ASTHMA, AN INFLAMMATORY LUNG DISEASE, is one of the most common chronic diseases of children. Common symptoms include recurrent wheezing, coughing, difficulty breathing, and/or tightness of the chest. Asthma attacks can range from mild to life threatening. There is no known cure for asthma, but it can be controlled by following a medical management plan and by reducing exposure to environmental "triggers," such as air pollution, pollen, tobacco smoke, pesticides, dust mites, furry pets, mold and certain chemicals. Asthma control is essential throughout life because, contrary to popular belief, you do not grow out of asthma. Health care providers can access the updated Asthma Guidelines at www.nhlbi.nih.gov

Asthma is a problem that needs to be addressed through policy change. Because the reduction of environmental triggers is an essential component of asthma control and prevention, individuals, communities, and policy makers must work together to find solutions. This report, which includes the latest data and research, will outline the problem of asthma in Merced County, describe some of the work being done to address the problem, and highlight some specific policy recommendations.

## Asthma Disparities in the San Joaquin Valley

- Asthma is among the most common chronic childhood diseases, affecting approximately 6.5 million children nationwide including 1.7 million children in California alone. The San Joaquin Valley (Valley), which includes Merced County, has four times the national average for asthma prevalence with one in five children under the age of 18 diagnosed with asthma.[1,2]
- The burden of asthma weighs heavily on children throughout the Valley. Approximately 9,600 children under the age of 18 living in the Valley visited an emergency room due to asthma-related issues of which 745 were children living in Merced County.[3]




High Levels of Ozone Pollution Persist in the San Joaquin Valley in Summer

## Environmental Triggers of Asthma: Outdoor Air Pollution

Air pollution is the number one environmental concern for the people of the Valley,[4] and for good reason – the Valley has some of the most polluted air in the country.[5] Air pollution endangers the health of residents, retards the growth of crops, and threatens the overall economy and quality of life in the region.

Contrary to popular belief, the majority of pollution in the Valley does not come from outside the area. In the Northern part of the Valley, including Merced County, 73% of pollution comes from local sources as opposed to only 27% that is transported from the Bay Area and Sacramento basins.[6]

The geography of the Valley acts as a trap for outdoor air pollution. Surrounding mountains trap airborne pollutants near the Valley floor where people live and breathe. Population growth also contributes to the problem, as more people bring more activities that contribute to poor air quality.

According to the Department of Finance[7], the Valley has the fastest growing population in California. As such, land-use is rising to the top of the agenda given increasingly limited resources and an economy historically rooted in agriculture. The built environment has a tremendous impact on quantity of and exposure to air pollution. In order to maintain healthy communities, smart growth principles must be the guiding principles of all land-use plans. Smart growth policies include: mixed land uses, walkable communities, preservation of open space, the enhancement of existing communities, and a variety of transportation choices.[8]

## Health Impacts of Air Pollution

Pollution impacts residents year-round with ozone (aka "smog") filling the Valley during the warm summer months, and particulate matter (PM 2.5) being the pollutant of concern in the Fall and Winter seasons. These two contaminants are devastating to lung and heart health and result in serious long term damage to our bodies that can even result in premature death. Ozone, caused from the combination of Nitrous Oxides (NOx) and Volatile Organic Compounds (VOCs) in heat can cause chest pain, shortness of breath, airway inflammation and asthma attacks.[9]

Fine particles, or PM 2.5, are microscopic solids or liquid droplets that can be breathed deep into the lungs and even absorbed into the bloodstream. When people are exposed to high levels of this type of pollution they are more likely to experience: asthma attacks, bronchitis, decreased lung function, heart attacks, and/or premature death.[10]

## Findings Related to Outdoor Pollution and Health

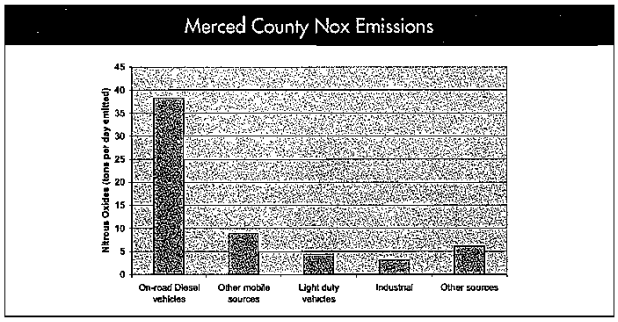
- Residential proximity to high-traffic roads has been associated with asthma hospitalizations, respiratory symptoms, and compromised lung function in children.[11]
- Children living in communities with higher concentrations of pollutants had lungs that developed and grew more slowly than other children and thus, had a reduced ability of transporting air through their lungs.[12]
- Children living in high ozone communities and who actively participated in sports were more likely to develop asthma than children who did not participate in sports.[13]
- Overall, Valley residents could expect annual benefits of $3.2 billion if both fine particulate matter and ozone Federal levels were attained.[14]

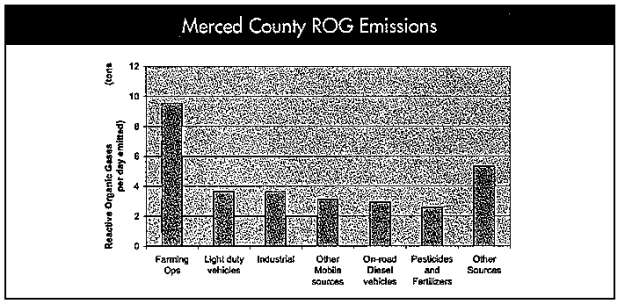
## Sources of Pollution

There is a wide array of pollution sources in Merced County. The top three sources of PM 2.5 in Merced

County in 2005 were heavy duty diesel trucks (14.8%), fugitive windblown dust from agricultural land and unpaved roads (13.2%), and farming operations including dust (11.8%).[15]

Ozone Precursors: The following two graphs detail the top contributors to ozone pollution in Merced County in 2006.[16]




## A Big Problem for Merced County

All of this pollution leads to the violation of health-based National and State Ambient Air Quality Standards in Merced County and the San Joaquin Valley Air Basin. For example, from 2000-2005 Merced County violated the State 8-hour ozone standard on 525 days and the National 8-hour ozone standard on 194 days![17]

### BECAUSE OF THIS:

- Merced County was ranked 8th in the national list of "People at Risk in 25 Most Ozone-Polluted Counties.[18]
- The city of Merced ranked 6th in the national list of "People at Risk in 25 Most Ozone-Polluted Cities".[19] Of the top 6 most ozone-polluted cities in the nation, four (Bakersfield, Visalia-Porterville, Fresno-Madera, and Merced) are located in the San Joaquin Valley.

## Keeping Children Healthy: Solutions in Schools

### OUTDOOR AIR QUALITY FLAG PROGRAM

In 2004, the Merced/Mariposa County Asthma Coalition launched the Outdoor Air Quality Flag Program at Merced County Office of Education campuses. Since then, this innovative program has spread to 21 of 22 public school districts in the County, private schools, hospitals, health centers, Head Start, and Migrant Head Start sites. In total, over 130 flags are flying on local flag poles that signify daily air pollution levels in the County.

Everyday, each participating school raises a flag that corresponds with the colors of the Air Quality Index. On a 'Good' air quality day the green flag is raised on the flag pole while a yellow flag goes up on a 'Moderate' day. An orange flag means the air is 'Unhealthy for Sensitive Groups' such as children, seniors, and people with heart and/or lung disease. A red flag means the air is 'Unhealthy' for everyone.

Given the frequency of unhealthy air days throughout the year in the Valley it is essential for Merced County residents, especially children, to take measures that reduce their exposure to harmful pollutants. To that end the MMCAC has created (in partnership with other organizations) the Active Indoor Recess (AIR) curriculum that outlines indoor activities students may do on poor outdoor air quality days during recess and PE.

### INDOOR AIR QUALITY PROGRAM

Merced County faces many challenges when addressing outdoor air quality issues; however, there are times when indoor air pollutants could be 2-5 times higher, and occasionally 100 times higher than outdoor levels. Poor indoor air quality (IAQ) can cause headaches, fatigue, sinus congestion, coughing, and sneezing; it can also promote the spread of airborne infectious diseases. Indoor air pollutants can be particularly harmful to students with allergies or asthma.[20]

The MMCAC collected data from 106 teachers through a "Teacher's Classroom Checklist" tool. The following data concludes there is more work to do in creating healthy classrooms and better IAQ in schools.

- 40% of participating teachers reported they did not know how their Heating, Ventilation, and Air Conditioning System worked or that they needed follow-up to ensure the unit's proper function.
- 21% of participating teachers reported there were water stains on their classroom ceilings or evidence of leaks or moisture.
- 24% of participating teachers reported their rooms were not dusted and swept or vacuumed regularly.
- 36% of participating teachers were unsure whether the cleaning products in their rooms were district approved or not.

The Merced/Mariposa County Asthma Coalition has partnered with four Merced County schools to evaluate campuses, educate teachers, and implement strategies

and policies that would improve indoor air quality in classrooms. By applying the EPA's Indoor Air Quality Tools for Schools program to existing policies and procedures, schools identify no-cost / low-cost solutions that promote an "asthma-friendly" classroom free of indoor environmental triggers. Some of these solutions may include maintaining the continual and uninterrupted exchange of air through Heating, Ventilation, and Air Conditioning systems, removal of scented products in School District classrooms (candles, air fresheners, perfumes, etc.), and the purchase and use of "Environmentally-Preferred Products" in custodial practices that emit the lowest amount of odor and Volatile Organic Compounds.

## POLICY RECOMMENDATIONS

Preventing people, especially children, from exposure to environmental asthma triggers, particularly indoor and outdoor air pollution, and reducing the amount of pollution being emitted into the ambient air are both critical in the reduction of the asthma burden in Merced County. Therefore, the Merced/Mariposa County Asthma Coalition proposes the following policy recommendations:

- Support expedient regional attainment of the 8-hour ozone and PM 2.5 State and National Ambient Air Quality Standards.
- Adopt standards in land use plans that incorporate smart growth principles and reject land uses that attract/emit high levels of pollutants, particularly diesel emissions, in order to protect the health of Merced County residents and downwind Valley communities.
- Adopt a uniform policy (ex. AIR) in all Merced County School Districts outlining appropriate indoor activities for unhealthy air days over Air Quality Index 100 as a component of school procedures and guidelines.
- Implement a comprehensive and effective Indoor Air Quality Management Plan in Merced County School Districts with set policies and procedures.

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17-1 The commenter states that the DEIR does not adequately address the project's impacts to air quality and does not identify and discuss all feasible measures that would reduce air quality impacts to a less-than-significant level. However, the commenter does not identify any specific topics that were not addressed in the air quality analysis, how the studies relied upon in the analysis are inadequate, which particular studies the comment refers to, or potential mitigation measures that should be added or modified in the DEIR. The commenter also states that "the full extent of the Valley's air quality public health crisis has not been taken into account on all levels of planning" but does not discuss which air quality-related public health concerns were not addressed. Section 4.2-1, Environmental Setting, presents information about the existing air quality conditions, the health effects of various pollutants, and the emissions inventory. Please also refer to Master Response 13.

17-2 The commenter indicates three main areas of concern, alleging first that the studies in the DEIR are dubious, second that additional feasible mitigation is available to reduce air quality impacts, and third the full extent of the Valley's air-quality-related health crisis was not fully considered. However, the commenter does not specify how the studies relied upon in the analysis are inadequate or which particular studies the comment refers to, and the commenter does not identify potential mitigation measures that should be added or modified in the DEIR. The commenter also states that "the full extent of the Valley's air quality public health crisis has not been taken into account on all levels of planning" but does not discuss which air quality-related public health concerns were not addressed. Section 4.2-1, Environmental Setting, presents information about the existing air quality conditions, the health effects of various pollutants, and the emissions inventory. Please also refer to Master Response 13.

17-3 The comment introduces a set of questions pertaining to the Draft EIR and suggests that the technical studies included in the Draft EIR are not reliable. The comment does not detail the issues with the studies in this comment, but the commenter's questions and issues are outlined in more detail in the comments that follow. The responses to the individual comments below address these issues.

17-4 The commenter raises concerns about the precise number of trucks that will use the facility, and indicates that the 2010 and 2030 traffic studies and mitigation measures are therefore flawed and useless. The trip generation forecast that was used in the traffic analysis was based on a survey of a similar facility in Apple Valley, CA, which has 1,201 employees and a similar fleet mix as the proposed facility in Merced. The survey of the Apple Valley facility analyzed the number of vehicles entering and exiting the site throughout the day and the type of vehicles (car, truck, etc.). The NOP's figure of 900 tractor/trailer trips per day was not based on an actual forecast of the project, and overstated the potential number of truck trips that are anticipated. No changes to the DEIR are required.

The actual PM peak hour of traffic was studied, with and without the proposed project. Therefore, the suggested mitigation for actual PM peak our traffic is considered adequate.

17-5 The commenter questions "How many idling trucks would sit at the intersection? How long would the trucks wait for the stoplight to change? How much more carcinogenic diesel soot would students, teachers, and staff breath?"

The traffic analysis in Section 4.11 of the DEIR discusses the affects of the project on area intersections. Table 4.11-14 summarizes the LOS of area intersections with the addition of project-generated vehicle trips, including truck trips. A "Delay" column is included in this table. As stated in note (a) of the table, "delay is in seconds per vehicle. For signalized intersections, delay is based on average stopped delay. For unsignalized intersections, delay is based at the worst approach for two-way stop controlled intersection." Please refer to the response to comment 92-3 for discussion concerning potential TAC emissions generated by off-site truck travel associated with the project. . With regard to the commenter's third question, Impact 4.2-4 and the supporting HRA analyzes the effects of on-site diesel truck emissions and other on-site TACs on nearby receptors, including schools, residents, and workers.

17-6 The commenter expresses concern about traffic backups onto SR 99 and traffic impacts to the Mission and SR 99 intersection. The DEIR's traffic operations analysis does not forecast that traffic would back up onto SR 99.

17-7 The commenter states that the intersection traffic analyses be redone to include a peak hour number for maximum truck trips. The existing and future condition at each of the studied intersections, for both the AM and PM peak hour of traffic, has been analyzed and properly assessed using the analysis procedures required by the City of Merced. No changes to the DEIR are required.

17-8 The comment discussed regional emissions from truck trips that would be associated with operation of the project. The comment incorrectly states that regional truck trip distances were provided by Wal-Mart. The distances of regional truck trips were estimated by the City's consultant based on the list of existing 49 stores that would be supported by the new distribution center instead of the existing distribution center in Apple Valley, CA or the existing distribution center in Red Bluff, CA. For each of these stores, the analysis compared the trip distance to the store's existing distribution center to the trip distance to the proposed distribution center in Merced. It also accounted for the average daily number of truck loads shipped to each store, how the route change would occur, and the change in vehicle miles traveled (VMT) inside the SJVAB. Under existing conditions, the average one-way trip distance inside the SJVAB would be approximately 106 miles. With operation of the proposed project, the average one-way trip distance would be approximately 83 miles.

17-9 The comment discussed regional emissions from truck trips that would be associated with operation of the project. The commenter states that the DEIR did not analyze those truck emissions that would be generated outside the SJVAB. Please refer to the response to comment 96B-27 and then the response to comment 17-11. The commenter acknowledges that truck trips associated with the operation of the project would travel in air basins outside the SJVAB and the commenter suggests that the City contact the air districts that regulate air quality in these air basins for comment on the DEIR. As explained in response to comment 96B-27, a net reduction in VMT associated with outbound delivery truck trips would expected for air basins outside the SJVAB. In addition, the VMT associated with inbound truck trips to the proposed distribution center could not be estimated without extensive speculation, as explained in response to comment 17-11.

17-10 The comment requests a list of the 49 existing retail stores that would be served by the proposed project. The Applicant has requested that the City not disclose which existing 49 stores would be served by the proposed project and the number of daily truck loads shipped to each store because this information is business sensitive. The locations of these 49 stores were used to determine the net change in VMT that would occur with implementation of the proposed distribution center in

Merced. The commenter's request for a list of these stores does not raise issues with the adequacy of the DEIR.

17-11 The commenter seeks clarity about why the net change in emissions by inbound receivable trips, as shown in Table 4.2-7 of the DEIR, total precisely zero. The commenter notes that those truck trips would still need to travel over 1 mile from State Route (SR) 99 to the project's entrance gate. The estimation of truck VMT under existing conditions and project conditions could not be estimated without extensive speculation. This is because detailed information about inbound receivable trips was not known at the time of the analysis, including the number of truck trips from each wholesale supplier or port from which goods are shipped to existing Wal-Mart distribution centers and the proposed distribution center, the location from which they are shipping products, and whether the origin of those shipments would be different for the proposed distribution center than the wholesale supplier's existing origin. Therefore, as stated in note 7 of Table 4.2-7, it was assumed that the average trip distance in the SJVAB for all inbound receivable truck trips that originate at ports or wholesale suppliers, with and without the proposed project, would be equal to the average existing trip distance of 106.2 miles between the 49 existing Wal-Mart stores that would be served by the Merced Distribution Center and the existing distribution center currently serving each of those stores; these existing centers are located in Red Bluff and Porterville. However, the trip distance of 106.2 miles is not as important as the assumption that the average trip distance of inbound delivery truck trips to the proposed distribution center would not be substantially different than the trip length of deliveries to the existing distribution centers in Red Bluff and Porterville. Without engaging in extensive speculation it is not possible to determine whether the VMT associated with trucks delivering wholesale goods to the proposed project would be greater or less than the VMT by trucks delivering to the existing distribution centers in Porterville and Red Bluff. (See Response to Comment 17-8 for additional information in VMT assumptions.)

17-12 The commenter states that the 7.3 in one million cancer risk level concluded in the HRA should not be dismissed as less than significant. As explained on page 4.2-27 of the DEIR, the threshold of significance used for evaluation of cancer risk is an "incremental increase in emissions of TACs that exceed 10 in 1 million for the carcinogenic risk," as recommended in SJVAPCD's Guidance for Air Dispersion Modeling (2006). This threshold of significance is also recommended by other air districts in California, including the Sacramento Metropolitan Air Quality Management District. Because the maximum incremental increase in cancer risk generated by the project would not exceed this threshold no mitigation measures are required to reduce this exposure level.

The commenter also states that the DEIR should analyze the localized impacts from off-site traffic-related emissions. The comment notes that the proposed truck route would pass within 1,000 feet of Pioneer Elementary School and would be adjacent to a planned Weaver School District elementary school site between Childs Avenue and Gerard Avenue. The discussion under Impact 4.11-2 on page 4.11-26 of the DEIR states that "no tractor trailer traffic is expected to travel past any of the three schools located near the intersections of Childs/Coffee [i.e., Weaver Elementary School], Gerard/Coffee [i.e., Pioneer Elementary School], and Parsons/Childs... However, there is a potential for trucks to stray from their expected routes occasionally. This could result in trucks passing through residential areas and past schools. This is a potentially significant impact that requires mitigation." Therefore, Mitigation Measure 4.11-2b requires the development and implementation of a truck route plan (See page 4.11-30). The measure requires that "tractor trailers approaching and departing from the distribution center shall be limited to the following roadways from SR 99 and SR 140: Campus Parkway, Mission Avenue west of Campus Parkway, Gerard Avenue east of Campus Parkway, and Tower Road. Wal-Mart shall regularly and routinely instruct its employees, contract truck drivers, and vendors of these roadway

limitations." This measure would prevent trucks form passing within 1,000 feet of any area schools, including the planned Weaver School District elementary school site between Childs Avenue and Gerard Avenue on the east side of the Crossing/Sandcastle residential development.

The commenter also states that the DEIR should evaluate the exposure of sensitive receptors to TACs under projected 2030 traffic conditions. In response, the discussion of cumulative impacts pertaining to TACs on page 6-5 has been altered as shown in Chapter 4, "Revisions and Corrections to the DEIR," section "Revisions to Section 6 'Cumulative and Growth-Inducing Impacts.'"

17-13 The commenter indicates that the traffic study ignores the buildout of the Heavy Industrial zoned land in southeast Merced, including a peaking power plant, and the cumulative health impacts of the proposed projects. The build out of the other proposed industrial uses in the area were considered in the DEIR's traffic analysis as part of the Cumulative Condition, which is based on the General Plan buildout of the area. It should be noted that the PUC rejected the application for the peaking power plant and no subsequent applications for peaking power plants are on file with the City.

17-14 The commenter expresses concern that the Air Impact Assessment (AIA) process amounts to inappropriate deferral of mitigation. Construction and operation of the proposed project shall comply with SJVAPCD's ISR rule (Rule 9510), as required by law. The applicant shall have an AIA application approved by the SJVAPCD before issuance of a building permit from the City of Merced. The AIA shall quantify operational $NO_X$ and $PM_{10}$ emissions associated with the project. This shall include the estimated operational baseline emissions (i.e., before mitigation), and the mitigated emissions for each applicable pollutant for the project, or each phase thereof, and shall quantify the offsite fee, if applicable. Any on-site reductions of CAP emissions must be both quantifiable and verifiable to be credited towards the requirements of the ISR Rule. The ISR rule states that the applicant shall include in the AIA application a completed proposed monitoring and reporting schedule (MRS) for on-site emission reduction measures selected that are not subject to other public agency enforcement. The MRS is a form listing on-site emission reduction measures committed to by the applicant that are not enforced by another public agency along with the implementation schedule and enforcement mechanism for each measure. A proposed MRS shall outline how the measures will be implemented and enforced, and will include, at minimum, a list of on-site emission reduction measures included; standards for determining compliance, such as funding, record keeping, reporting, installation, and/or contracting; a reporting schedule; a monitoring schedule; and identification of the responsible entity for implementation. Upon completion of monitoring and reporting, SJVPACD shall provide to the applicant, the public agency, and make available to the public, an MRS Compliance letter. The DEIR does not defer mitigation; rather it clearly defines the enforcing agency and the timeline for implementation of the mitigation measures, which are based on an existing SJVAPCD (Rule 9510). Please also refer to response to comment 16-19.

The Merced/Mariposa County Asthma Coalition (MMCAC) requests that the public be able to participate and consult with SJVAPCD in the development of the AIA that would be required by Mitigation Measure 4.2-2a and the development of the emissions reduction agreement, which is required by Mitigation Measure 4.2-2e. It will be up to the SJVAPCD to define that process and to determine the level of public involvement.

17-15 The commenter encourages the use of onsite mitigation to reduce actual emissions from vehicles entering and exiting the project site. The DEIR includes onsite mitigation in the form of measures 4.2-2b and 4.2-2c. In particular, mitigation measure 4.2-2c requires the applicant to participate in EPA's SmartWay Transport Partnership, which would ensure that the fleet of Wal-Mart-owned

trucks consists of energy efficient trucks resulting in a reduction in truck-generated emissions. The commenter does not provide any specific ideas about additional on-site mitigation. Please also refer to response to comment 9-2.

17-16 The MMCAC states that "a majority of trucks using the [distribution center] would be non-Wal-Mart trucks. We encourage the development of an enforceable mitigation program that monitors all trucks using the facility." Please refer to the response to comments 9-2 and 12-5.

17-17 The MMCAC states that "the SJVAPCD should require Wal-Mart to mitigation each type of criteria pollutant to zero for the life of the project." This comment is not directed to the City, but rather to SJVAPCD. Please refer to Master Response 13 for discussion about the relationship between SJVAPCD's thresholds of significance, SJVAPCD's air quality planning efforts, and public health concerns related to air quality in the SJVAB.

The MMCAC disputes "the DEIR's claim that SJVAPCD 'has not identified mass emission thresholds for operational emissions of PM10 and PM2.5.'" With regard to a mass emission threshold for PM10, please refer to response to comment 21-4. SJVAPCD has not developed a mass emission threshold for PM2.5.

17-18 The MMCAC states that "given the extreme air quality public health crisis that our members experience on a daily basis, the [SJVAPCD] should require 2:1 mitigation per ton of pollutant." This comment is not directed to the City, but rather to SJVAPCD. Please refer to response to comment 118-5.

17-19 The MMCAC states that "if the City of Merced is going to monitor the voluntary agreement mitigation measures, we ask that the [SJVAPCD] and California Air Resources Board staff train City of Merced staff in appropriate fields to assist in gaining expertise in recognizing and mitigating criteria pollutants." The development of the AIA required by Mitigation Measure 4.2-2a and the development of the emissions reduction agreement required by Mitigation Measure 4.2-2e would not necessitate ongoing enforcement or monitoring by the City of Merced. Text has been added to the language of Mitigation Measures 4.2-2a and 4.2-2e to clarify the enforcement mechanism of these measures. Please refer to response to comment 17-14.

17-20 The MMCAC states that "if Wal-Mart chooses to pay an in-lieu fee, we request 1) that PM emissions be mitigated at a 2:1 ratio and 2) that on-site fees be directed towards helping Merced residents cope with the real world health impacts of local PM emissions." Please refer to response to comment 118-5 regarding item 1. With regard to item 2, providing funding and or services to help affected citizens cope with an environmental impact would not be considered a reduction of that impact; it would not reduce emissions of CAPs and precursors in the SJVAB. The development of the AIA required by Mitigation Measure 4.2-2a and the development of the emissions reduction agreement required by Mitigation Measure 4.2-2e would reduce emissions of CAPs and precursors in the SJVAB to a less-than-significant level.

17-21 The MMCAC states that "the DEIR should also discuss how this project may interfere with regional or countywide emission reduction goals set under SB 375." The commenter also states that "these goals should be included in the City of Merced's updated General Plan."

Senate Bill (SB) 375, signed in September 2008 (Chapter 728, Statutes of 2008), aligns regional transportation planning efforts, regional GHG reduction targets, and land use and housing allocation. SB 375 requires metropolitan planning organizations (MPOs) to adopt a sustainable communities strategy (SCS) or alternative planning strategy (APS) that will prescribe land use allocation in that MPOs regional transportation plan. ARB, in consultation with MPOs, will provide each affected region with reduction targets for GHGs emitted by passenger cars and light

trucks in the region for the years 2020 and 2035. These reduction targets will be updated every 8 years but can be updated every 4 years if advancements in emissions technologies affect the reduction strategies to achieve the targets. ARB is also charged with reviewing each MPO's SCS or APS for consistency with its assigned targets. If MPOs do not meet the GHG reduction targets, transportation projects will not be eligible for funding programmed after January 1, 2012.

This law also extends the minimum time period for the regional housing needs allocation cycle from 5 years to 8 years for local governments located within an MPO that meets certain requirements. City or county land use policies (including general plans) are not required to be consistent with the regional transportation plan (and associated SCS or APS). However, new provisions of CEQA would incentivize (through streamlining and other provisions) qualified projects that are consistent with an approved SCS or APS, categorized as "transit priority projects."

Emission reduction goals have not been set for the local MPO, or any other MPO in California pursuant to SB 375; therefore, the project cannot conflict because no goals have been set.

17-22 The MMCAC states that "the current City of Merced Vision 2015 General Plan, written in 1995-6 and approved in 1997, is out-of-date" and that "the City is out of compliance with the letter and intent of AB 170." The air quality analysis in the DEIR (See Section 4.2) does not rely on significance determinations made in the General Plan EIR; therefore, the comment does not address the adequacy of the DEIR for the proposed project. Information about the General Plan is included in the regulatory setting of the air quality analysis for disclosure purposes only. The MMCAC also states that "this project contradicts the 'Toxic and Hazardous Emissions' section of the SJVAPCD's Air Quality Guidelines for General Plans." The comment fails to provide reasoning that supports this claim. By addressing the project's TAC emissions and their potential health impact to receptors in the surrounding community in Impact 4.2-4, which concluded a less-than-significant impact, the City has fulfilled the guidance provided in SJVAPCD's Air Quality Guidelines for General Plans, available at http://www.valleyair.org/notices/Docs/priorto2008/8-2-05/Entire-AQGGP.pdf). The City has ensured that the proposed project would be "located an adequate distance from residential areas and other sensitive receptors" as stated in Policy 28.

17-23 The MMCAC states that "as a good-faith commitment and in order to reduce Vehicle Miles Traveled (VMTs) as required by SB 375, the Wal-Mart Corporation must hire 90% of all [distribution center] employees from Merced County (residents who live in Merced County prior to employment)." This comment is noted. The MMCAC's concern about the employees who would work at the proposed project does not raise issues with the adequacy of the DEIR. The comment is noted. Please refer to response to comment 17-21 regarding the SB 375. Please also refer to response to comment 96B-27 regarding the anticipated net change in truck VMT that would result from the proposed project.

17-24 The MMCAC provides a list of mitigation measures to be implemented that would reduce operational emissions of CAPs and precursors. However, the commenter does not argue that the mitigation measures listed in the DEIR are insufficient or reasons why additional mitigation is needed. Impact 4.2-2 regarding operational emissions of CAPs and precursors was found to be significant and mitigation measures 4.2-2a through 4.2-2e were proposed to minimize this impact to a less-than-significant level. Impact 4.2-3 regarding localized mobile-source emissions of carbon monoxide was found to be less than significant. Impact 4.2-4 regarding localized exposure of sensitive receptors to emissions of toxic air contaminants was found to be less than significant.

The MMCAC also expresses concerns about the relationship between project-related emissions and asthma and other respiratory health concerns in the region. Please refer to Master Response 13.

The MMCAC also requests that mitigation require the Wal-Mart to fund health and medical service programs to local citizens with asthma or other air quality-related medical conditions. However, providing funding and or services to help affected citizens cope with an environmental impact would not be considered a reduction of that impact; it would not reduce emissions of CAPs and precursors in the SJVAB. Mitigation Measures 4.2-1a through 4.2-1e and 4.2-2a through 4.2-2e would reduce emissions of CAPs and precursors in the SJVAB to a less-than-significant level. Therefore, the proposed project would not conflict with SJVAPCD's air quality planning efforts for the SJVAB.

17-25 The MMCAC states that "any mitigation measures as a result of this project should be binding with a clear timetable for implementation and benchmarks to measure their success." All mitigation measures in the DEIR are binding, as discussed in response to comment 105-1. Additional text has been implemented to the mitigation measures regarding air pollutant emissions in Section 4.2 to provide clarity about the timing, responsibility, and enforcement mechanism of each measure. Please refer to Section 4.2 for text changes and additions.

17-26 The MMCAC states that the measure in Mitigation Measure 4.2-2d which states that "The project shall include as many clean alternative energy features as possible to promote energy self-sufficiency (e.g., photovoltaic cells, solar thermal electricity systems, small wind turbines)" is too vague. The City chose to allow flexibility in the choice of technologies because technology, by nature, changes over time, and what might be the best available technology today may not be the best in several years if this project is built, or after 10 years of operation.

MMCAC also requests that this measure state that natural gas is not considered an alternative energy feature. The DEIR does not suggest that natural gas is an alternative energy source because natural gas is widely used in buildings throughout California.

MMCAC suggests that language be added to Mitigation Measure 4.2-2d that requires the applicant's written report regarding the feasibility of implementing additional operational on-site emission reduction measures, which must be submitted to the City, to also be made available for public comment. MMAC, however, does not provide reasons why this would make Mitigation Measure 4.2-2d more effective or potentially result in emissions reductions that would not otherwise occur. MMAC also suggests that the report must be approved by "knowledgeable independent experts" to determine "whether the additional measures are truly technologically or economically infeasible. The City of Merced, the CEQA Lead Agency, is qualified to determine feasibility of mitigation measures. However, the text of Mitigation Measure 4.2-2d has been modified to require the mitigation monitoring program to include the guidance of a sustainability expert. Please see Section 4.4 of this FEIR for the specific text revisions.

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