

The UCLA Population Studies of CORD: X. A Cohort Study of Changes in Respiratory Function Associated with Chronic Exposure to SO_x, NO_x, and Hydrocarbons

ABSTRACT

Two never-smoking cohorts in Southern California, one in Lancaster (N = 2340) exposed only to moderate levels of oxidants and the other in Long Beach (N = 1326) exposed to high levels of SO_x, NO₂, hydrocarbons and particulates completed spirometry and the single-breath nitrogen test five to six years apart. Forty-seven percent and 45 percent of the participants were retested. Mean results at baseline for those tested and not retested were similar. Loss to follow-up was primarily due to moving (39 percent and 47 percent). Every difference of consequence indicated greater deterioration in lung function in Long Beach. The level of significance of the difference was greatest, even in the youngest age groups, for $\Delta N_{2,750-1,250}$, suggesting that the earliest site of impairment may occur in the small airways. Greater deterioration in spirometric parameters was observed in every age group in Long Beach females above seven years of age at baseline and in Long Beach males above 15 years of age, suggesting that chronic exposure to the pollutant mix occurring in Long Beach ultimately adversely affects the large airways as well as small airways. (*Am J Public Health* 1991;81:350-359)

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Introduction

The relationship of temporary high levels of SO_x and particulates to health has been well documented by episodes such as those reported in the Meuse Valley, Donora, and London. A higher prevalence of symptoms of chronic obstructive respiratory disease and/or impaired lung function has been reported in cross-sectional studies in areas exposed to high levels of SO_x, NO_x, and/or particulates,¹⁻⁴ while in other studies a relationship has not been observed.⁵ A number of cohort studies have also been completed, especially in adults.⁶⁻¹⁴ The major problems encountered in cohort studies have been maintaining continuous measurement of pollutant levels and controlling for confounding factors which may change. These studies have depended primarily on the use of spirometry for measurement of lung function because of the difficulties associated with doing population studies using possibly more sensitive tests such as the single-breath nitrogen test. There is considerable evidence from experimental studies of both animals and humans that SO₂ and particulate sulfates may be responsible for bronchoconstriction,¹⁵⁻²⁴ possibly mediated through histamine release and subsequent action on bronchial smooth muscle.²⁵ A number of these studies have shown such effects at concentrations that occur in ambient air in some urban areas in the United States.

Previously, we reported a greater rate of deterioration in spirometric indices of the single-breath nitrogen test in residents chronically exposed to high levels of oxidants, oxides of nitrogen, sulfate, and particulates compared to an area exposed to low levels of these pollutants.²⁶

In this paper we compare changes over a five- to six-year period in spirometric tests and the single-breath nitrogen test in never-smoking residents of an area chronically exposed to high levels of SO₂, sulfates, NO_x, and hydrocarbons but low levels of oxidants with changes to those in residents of another area exposed to low levels of these pollutants to which comparisons to the oxidant-polluted community were made in the previous paper.

Methods

Establishment of Cohorts

Study areas were selected in Lancaster (located 75 miles north of downtown Los Angeles) which historically has been chronically exposed to moderate levels of photochemical oxidants and very low levels of other pollutants and in Long

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TABLE 1—Demographic Characteristics of Study Census Tracts in Lancaster and Long Beach*

Characteristics	Lancaster	Long Beach
Total residents, all ages	7,069	4,992
White (non-Spanish-surnamed) (%)	6,430 (91.0)	4,939 (98.9)
Spanish-surnamed (%)	434 (6.1)	0 (0.0)
Black (%)	91 (1.3)	3 (0.1)
Other (%)	114 (1.6)	50 (1.0)
Total 7+ years of age	6,121	4,691
Median income	\$11,631	\$11,474
Number of housing units	2,238	2,197
Proportion of homeowners (%)	63	64
Median home value	\$18,600	\$23,400

*According to the 1970 census.

Beach (located approximately 30 miles southwest of downtown Los Angeles) which has been chronically exposed to high levels of sulfur dioxide, sulfates, oxides of nitrogen, and probably hydrocarbons. Using 1970 census information, study areas were selected that were demographically similar, each of which contained an established air quality monitoring station. A comparison of the demographic characteristics of the two study areas according to the 1970 census is shown in Table 1. Although the Long Beach study area included a lower proportion of non-Whites, all comparisons in this paper are restricted to White, non-Spanish-surnamed residents who never smoked in order to reduce non-comparability between the cohorts. Participants were considered "never smokers" if they had never smoked more than one cigarette per day. Participants who reported smoking at either the baseline or follow-up examination were excluded from the analysis.

Cross-sectional studies conducted in the Lancaster study area in 1973–74 and in the Long Beach study area in 1974–75 demonstrated poorer lung function in Long Beach.²⁷ Concurrent testing was not possible due to funding limitations. Pollutant levels in Long Beach, however, remained similar over this period of time. Details of the recruitment of the study areas have been reported previously.^{26–30} Briefly, all the heads of households were identified through reverse telephone directories and voter registration files. Before explanatory letters were sent out, descriptive information regarding the program was presented in the local media. Following the mailing of individualized letters, a neighborhood representative set up an appointment to complete a roster of all household members seven years of age

and older and to arrange appointments for lung function testing at the Mobile Lung Function Laboratory, which was located within walking distance.

At the Mobile Laboratory, an interview schedule modified from the National Heart, Lung and Blood Institute Questionnaire was administered; this contained questions concerning respiratory symptoms, and history of respiratory disease, occupation, smoking, and residence. Height and weight were recorded, and the following pulmonary function tests were done: body plethysmography; single-breath nitrogen washout curve, including calculation of $\Delta N_{2,750-1250}$ * and closing volume; and electronic spirometry measurement with permanent recording of the entire maximal expiratory flow volume relationship on computer tape. The test equipment used was the same for all the testing except for the recorder for the spirometer. The new recorder, however, was thoroughly calibrated to the old recorder before being put into use. Details of the instrumentation used and the procedures followed are contained in previous papers.^{28,29} Results of body plethysmographic tests were inconsistent at baseline; thus, changes in these tests could not be determined with confidence. Details of the procedures for administering the single-breath nitrogen test and spirometry are given in Appendix A.

Retesting of the Cohorts

Approximately five years in Lancaster and six years in Long Beach after the baseline studies, retesting in each of the study areas was completed (1978–79 in Lancaster and 1980–81 in Long Beach).

*Change in the nitrogen concentration between 750 and 1250 cc of expired air.

Results, however, have all been expressed as annualized rates of change. In the interval between baseline testing and retesting, addresses had been updated through periodic mailings to all participants. Study participants were recontacted and invited to be retested in the same month in which they had originally been tested. Individuals who had moved but remained within a reasonable distance were also encouraged to undergo retesting at the Mobile Laboratory. Intensive efforts were made to persuade all participants to be retested, including call back within one day of individuals who did not keep their appointments at the Mobile Lung Function Laboratory. The procedures for retesting were identical to those used at baseline; the tests were administered in the same sequence and in the same manner.

Individuals who had moved out of the original study area were requested to undergo retesting at the Mobile Laboratory if they visited the Southern California area. Participants who had moved outside of the study area to a known address and who could not be retested were asked to complete a brief questionnaire on respiratory symptoms, smoking, and reasons for moving from the study area, including a final question that asked if the reason for moving was related to respiratory problems.

Validation and Quality Control

Procedures were implemented to calibrate and maintain the reliability of the lung function tests and to assess the effects of concurrent levels of air pollutants. These have been described in detail previously.^{29,31} Briefly, they included the following:

Calibration: At the beginning of the testing period in each area the results of lung function testing in the Mobile Laboratory were compared with results obtained from the UCLA (University of California at Los Angeles) Pulmonary Function Laboratory on 10 to 20 participants who were tested on the same day in both laboratories in a randomized sequence. At the beginning of each day's testing in the field and at regular intervals during the testing, the test equipment was recalibrated using standard procedures. In addition, calibration values were recorded on computer tape and evaluated at the end of each test day at UCLA. The Mobile Laboratory was immediately notified of any signs of error or "drift" so that if needed, the instruments could be adjusted before testing commenced the next day. Individuals tested the previous day were

TABLE 2—Average Number of Days on which Specified Pollutants Were Above California Ambient Air Quality Standards and Means of Daily Peak Hourly Values, 1972–81

Pollutant	Lancaster	Long Beach
SO ₂		
Days ≥ 0.05 ppm recorded 1978–81*	0	5
mean (ppm)	.01	.04
Oxidants		
Days ≥ 0.08 ppm for 1972–77, ≥ 0.10 ppm for 1978–81	92	18
mean (ppm)	.07	.04
NO ₂		
Days ≥ 0.25 ppm	0	23
mean (ppm)	.03	.11
SO ₄		
Days (not recorded)	—	—
mean (μg/m ³ , 24 hour totals measured every 6th day, 1977–81)	4.3 (4.3)**	11.3 (11.6)**
Total Suspended Particulates (μg/m ³)		
Days ≥ 100 μg/m ³ :		
recorded Lancaster 1978–81	18 (19)**	—
recorded Long Beach 1976–81	—	27 (24)**
annual geometric mean (μg/m ³)	85 (76.1)**	101 (98.6)**
*24 hour standard		
**median value		

asked to undergo retesting; results for those not retested were deleted.

Reliability and Validity: The reliability of the test procedures was evaluated by requesting every tenth individual completing lung function testing to undergo repeat lung function testing within 20 minutes and comparing the results. In addition, a 3 percent probability sample of participants was asked to undergo additional testing at the UCLA Pulmonary Function Laboratory, usually within two to three months of field testing. The results of the tests in the two laboratories were compared.^{26,29}

Effect of Concurrent Pollutant Levels: The possible effect of levels of air pollutants on the day of testing was evaluated by comparing lung function test results in 40 participants in Lancaster and 35 participants in Long Beach tested three times at four-month intervals in each study area. In addition, O/P (observed/predicted — adjusted for age, height, and weight) forced expiratory volume in one second (FEV₁) for all of the adult participants retested was analyzed relative to the level of pollutants recorded for the day on which their test was performed.³⁰

Levels of Air Pollutants

Monitoring stations of the Southern California Air Quality Monitoring District located in the two study areas continuously recorded levels of total oxidants, nitric oxide, nitrogen dioxide, total oxides of

nitrogen, total hydrocarbons (Lancaster only), and sulfur dioxide.³¹ In addition, 24-hour totals for total suspended particulates (TSP) and for sulfates (at six-day intervals) were monitored. The maximum hourly level for oxidants, SO₂ and NO_x, and the 24-hour total for TSP and SO₄, as recorded at the respective monitoring station on the day of testing, were attached to each individual's computer record. All measurements met both the California and federal Environmental Protection Agency guidelines for acceptability of testing procedures for these pollutants.

Results

Levels of Pollutants during the Study Period

The annual means of the daily peak hourly values for SO₂, oxidants, NO₂, and of the 24-hour total value for SO₄ and TSP over the 10-year period are shown in Table 2. The table also gives the average number of days per year on which SO₂, oxidants, NO₂, and TSP exceeded the California ambient air quality standard. Days exceeding these levels were not recorded for all years between 1972 and 1981.^{31,32} The years contributing to the determination of the mean number of days are given separately for each pollutant. In terms of both days above California ambient air quality standards and means of the daily peak

hourly levels, the largest differences in recorded pollutants were in levels of NO₂. Levels of all indicated pollutants except oxidants, however, were higher in Long Beach. On the other hand, there was a five-fold greater number of days on which oxidants exceeded 0.08 or 0.10 ppm in Lancaster, but less than a two-fold difference in the annual means of the daily peak hourly levels between the two communities. Although the level of oxidants in Lancaster was lower than in most other areas of the Southern California air basin, it was nonetheless higher than in most urban areas in the United States. Unfortunately, levels of hydrocarbons were not measured at the Long Beach monitoring station, but the location of the study area directly downwind from the major oil refining area in Los Angeles and the results of interpolation from adjacent monitoring stations suggest that levels of hydrocarbons were also very high in the Long Beach study area.

Response Rates

Response rates for the two cohorts are given in Table 3. The proportion remaining in the study area who completed all of the lung function tests was reasonably high in both areas (75 percent and 77 percent). An additional 6 percent and 9 percent, respectively, completed only the questionnaire. One percent of participants in both areas were known to have died. The major problem in follow-up was the high proportion of individuals who moved out of the study area: 39 percent (910/2340) in Lancaster and 47 percent (629/1326) in Long Beach. In Lancaster, only 12 percent (270/2340) and in Long Beach only 7 percent (94/1326) of participants refused to be retested. The overall retest rate, excluding deaths, for persons completing all lung function tests was 47 percent for Lancaster and 45 percent for Long Beach.

The proportions retested, stratified by age, sex, and place of residence, are given in Table 4. The proportion retested tended to be lower for individuals who were 11–24 years of age at baseline testing, a finding not unexpected in this highly mobile age group leaving home for college and jobs over the five- to six-year interval between baseline testing and retesting.

Because the overall retest rate was not as high as we would have liked, a comparison was made in Table 5 of the lung function test results at baseline among those who completed retesting and those who did not. The high mean observed/predicted values at baseline for those retested reflects the fact that they repre-

TABLE 3—Retest Status of Never Smokers 7–59 Years of Age at Baseline

Residence at Baseline	Total Tested at Baseline N	Retested				Not Retested					
		Lung Function Test		Questionnaire Only		Deaths		Refused		Lost	
		N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Lancaster											
Study area	1430	1061	(74)	80	(6)	19	(1)	270	(19)	—	—
Moved	910	38	(4)	325	(36)	—	—	—	—	547	(60)
Total	2340	1099	(47)			19	(1)				
Long Beach											
Study area	697	523	(75)	62	(9)	18	(3)	94	(13)	—	—
Moved	629	63	(10)	136	(21)	—	—	—	—	430	(68)
Total	1326	586	(44)			18	(1)				

TABLE 4—Percent of Never Smokers* Retested, Stratified by Age, Sex, and Place of Residence

Sex/Age (years) [†]	Lancaster		Long Beach	
	Tested at Baseline N	% Retested	Tested at Baseline N	% Retested
Males				
7–10	210	50	87	40
11–14	217	47	67	27
15–18	140	26	50	32
19–24	61	38	63	38
25–59	262	54	238	53
Females				
7–10	162	46	77	44
11–14	207	51	73	36
15–18	158	35	52	39
19–24	82	37	89	42
25–59	482	55	401	48

*White, non-Spanish-surnamed only, 7–59 years of age at baseline; had not changed job or residence because of a respiratory problem; FEV₁ exists at both times.
[†]Age at baseline.

sent volunteers who survived for five to six years and were still willing to be retested. Thus, the mean of their observed/predicted test performance at baseline does not reflect the mean for the entire group tested at baseline.

Validity of Results

The mean test/retest results for those 10 percent immediately retested were within 5 percent for the major spirometric indices. Regression analysis of the level of air pollutant on day of testing and the mean test value for FEV₁ for that day for all participants revealed no statistically significant correlations. Of the 24 comparisons made of results of FVC, FEV₁, FEF_{25–75}, FEF_{50–75}, $\Delta N_{2750-1250}$, and closing volume in the two groups of participants tested at different seasons of the year, only one, $\Delta N_{2750-1250}$ was significant at the $p < 0.04$ level; equivalent to chance

for this number of comparisons. Mean test results in the cohort retested in three different seasons were not significantly different.

An estimate of the possible impact of errors resulting from the testing procedures in the mobile lung function laboratory was calculated by comparing the results of FEV₁ in the 3 percent probability sample of adults tested in both the mobile and the UCLA lung function laboratories. (Levels of pollution at UCLA fall between those in Lancaster and Long Beach except that the levels of oxidants are higher at UCLA than in either study area.) The mean interval between testing in the mobile and UCLA laboratories was several months.

The difference between FEV₁ values at the Mobile Laboratory were greater at T₂ (retesting) than at T₁ (baseline) in both communities although mobile laboratory

values were lower at both examinations. If the UCLA laboratory results represented the true values, then the greater inter-laboratory differences at T₂ than at T₁ suggest that the annual decline in FEV₁ as measured in the field laboratory might have been exaggerated. Furthermore, comparison between the two communities of the inter-laboratory differences at T₂ versus T₁ suggests that this potential exaggeration of the annual decrement in FEV₁ was slightly greater in Long Beach (–13 ml/year, SE \pm 7 ml/year) than in Lancaster (–2 ml/year, SE \pm 7 ml/year). These decrements were not statistically different. Further, these differences observed in the 3 percent probability sample may not have existed in the entire group tested. The response rate for retesting of the 3 percent probability sample at T₂ was less than 50 percent.

Changes in Lung Function Tests

The means of the individual changes in tests are shown in Table 6A, for males and females 25–59 years of age, and stratified into five age groups for males (Table 6B) and females (Table 6C) 7–24 years of age at baseline. Non-adults were stratified to separate the growth phase of childhood from the declining trend in lung function which begins in late adolescence, as we have reported previously.³³ The levels of significance of differences between results in the two areas are shown in Table 7 for those age-and-sex-specific groups in which the probability was less than .05.

Changes for $\Delta N_{2750-1250}$ and the spirometric indices except V₇₅ were significantly worse in Long Beach participants 25–59 years. The level of significance for the difference in baseline and follow-up test results was highest for the single-breath nitrogen test. The levels of signifi-

TABLE 5—Means and Standard Errors of Spirometric and $\Delta N_{2750-1250}$ Tests at Baseline for Never Smokers Tested and Not Retested*

Test/Unit/ Residence	Retested		Died	Not Retested
	Lung Function Tests	Questionnaire only		
Number†				
Lancaster	829	311	19	740
Long Beach	499	156	18	516
FEV ₁ (0/P%)**				
Lancaster	100 ± 0.5	100 ± 1.0	87 ± 4.8	99 ± .84
Long Beach	103 ± 0.7	101 ± 1.6	90 ± 6.5	101 ± 1.05
FEF _{25-75%} (0/P%)**				
Lancaster	92 ± 1.7	96 ± 2.6	100 ± 6.8	91 ± 2.21
Long Beach	89 ± 2.0	94 ± 4.3	91 ± 11.7	85 ± 2.99
\dot{V}_{50} (l/sec)				
Lancaster	4.1 ± 0.06	4.3 ± 0.09	4.4 ± 0.40	4.2 ± .08
Long Beach	4.1 ± 0.07	4.4 ± 0.12	4.4 ± 0.49	4.1 ± .12
\dot{V}_{75} (l/sec)				
Lancaster	1.7 ± 0.03	1.7 ± 0.04	1.8 ± 0.18	1.7 ± .04
Long Beach	1.5 ± 0.04	1.7 ± 0.07	1.6 ± 0.22	1.4 ± .06
$\Delta N_{2750-1250}$ (%)				
Lancaster	0.71 ± 0.03	0.75 ± 0.04	1.33 ± 0.18	.79 ± .09
Long Beach	0.94 ± 0.04	0.73 ± 0.05	0.81 ± 0.17	.91 ± .05

*White, non-Spanish-surnamed only; 7-59 years of age at baseline; had not changed job or residence because of a respiratory problem.
 †Minimum number in groups.
 **Expected values derived from previously reported equations (reference 28).

TABLE 6A—Means of Annual Change in Lung Function Tests Results between Baseline and Retest 5-6 Years Later in Participants* 25-59 Years Who Never Smoked

	FEV ₁	FVC	FEF _{25-75%}	\dot{V}_{50}	\dot{V}_{75}	$\Delta N_{2750-1250}$
Males						
Lancaster (N = 132)	-51 ^{±5**}	-57 ^{±7}	-54 ^{±12}	-75 ^{±21}	-44 ^{±9}	-1.9 ^{±1.2}
Long Beach (N = 120)	-66 ^{±4}	-83 ^{±6}	-93 ^{±10}	-121 ^{±14}	-53 ^{±8}	3.2 ^{±0.9}
Females						
Lancaster (N = 259)	-36 ^{±3}	-41 ^{±4}	-56 ^{±7}	-83 ^{±9}	-40 ^{±7}	-1.5 ^{±0.8}
Long Beach (N = 188)	-50 ^{±3}	-61 ^{±4}	-78 ^{±7}	-111 ^{±8}	-40 ^{±5}	6.6 ^{±1.2}

*White, non-Spanish-surnamed only, had not changed job or residence because of a respiratory problem. FEV₁ exists at both times.
 **Mean of annualized 5-year change; mean = (T2-T1/elapsed months × 12 ± standard error).

cance of the differences were higher for most tests for adult women than for men except for the FEF_{25-75%}.

Among non-adults, a significantly less favorable change in the results of the single-breath nitrogen test was observed in the youngest age group (7-10 years) for both males and females in Long Beach. A less favorable change in the results of the single-breath nitrogen test was observed in every age group under 25 years in Long Beach, but was not statistically significant in the 11-14 and 19-24 year groups among males and in the 15-18 year old group in females.

Among non-adult females the changes in spirometry were worse among Long Beach participants in every age group except for the \dot{V}_{75} in the 7-10 year group and reached statistical significance for at least one spirometric test in every

age stratum (Table 6C). Among males under 15 years, however, spirometry was not consistently worse in Long Beach participants. Above 15 years spirometry was consistently worse in Long Beach male participants, but did not reach statistical significance in the 15-18 year group. Above 19 years the results were significantly worse in Long Beach participants for all the spirometric indices except \dot{V}_{75} .

In every instance in which a statistically significant difference was observed the rate of change was worse among residents of the more polluted area, Long Beach. These included tests believed to reflect both small and large airways function. A significantly greater rate of deterioration was observed at an earlier age among females than among males.

Discussion

Although cohort studies provide the only absolute measures of risk in human populations, a number of problems arise in successfully completing them. Probably the most important is to achieve follow-up of a high proportion of participants. The proportion of all living participants completely retested in this study was low (47 percent and 45 percent in Lancaster and Long Beach, respectively). The major reason for not being retested, however, was not refusal, but migration out of the study area (39 percent and 47 percent, respectively.) The proportion completely retested of those remaining in the study areas was relatively high (75 percent and 77 percent). In the interval between baseline and retesting only a small percentage of participants moved

TABLE 6B—Means of Annual Change in Lung Function Test Results Between Baseline and Retest 5–6 Years Later in Male Participants* 7–24 Years Who Never Smoked

Males	FEV ₁ (ml)	FVC (ml)	FEF _{25–75%} (ml/sec)	\dot{V}_{50} (ml/sec)	\dot{V}_{75} (ml/sec)	$\Delta N_{2750-1250}$ (% × 100)
7–10 Years						
Lancaster (N = 96)	287 ^{±11†}	338 ^{±14}	297 ^{±18}	305 ^{±19}	154 ^{±14}	-6.7 ^{±1.3}
Long Beach (N = 32)	286 ^{±16}	327 ^{±17}	307 ^{±29}	320 ^{±30}	181 ^{±22}	-0.4 ^{±1.5}
11–14 Years						
Lancaster (N = 82)	309 ^{±11}	351 ^{±14}	338 ^{±19}	331 ^{±21}	172 ^{±18}	-1.5 ^{±1.0}
Long Beach (N = 14)	313 ^{±25}	352 ^{±32}	335 ^{±30}	329 ^{±44}	182 ^{±24}	-0.6 ^{±2.1}
15–18 Years						
Lancaster (N = 26)	64 ^{±17}	75 ^{±17}	48 ^{±30}	50 ^{±38}	-15 ^{±36}	-4.0 ^{±2.4}
Long Beach (N = 16)	37 ^{±14}	39 ^{±18}	0 ^{±23}	-10 ^{±27}	-20 ^{±14}	3.2 ^{±2.1}
19–24 Years						
Lancaster (N = 21)	-16 ^{±13}	-12 ^{±14}	-8 ^{±20}	0 ^{±32}	-45 ^{±21}	-1.8 ^{±2.4}
Long Beach (N = 23)	-70 ^{±13}	-72 ^{±15}	-125 ^{±26}	-149 ^{±40}	-90 ^{±18}	0.4 ^{±0.9}

*White, non-Spanish-surnamed only, had not changed job or residence because of a respiratory problem. FEV₁ exists at both times.

†Mean of annualized 5-year change; mean = (T2-T1/elapsed months × 12 standard error).

TABLE 6C—Means of Annual Change in Lung Function Test Results between Baseline and Retest 5–6 Years Later in Female Participants* 7–24 Years Who Never Smoked

Females	FEV ₁ (ml)	FVC (ml)	FEF _{25–75%} (ml/sec)	\dot{V}_{50} (ml/sec)	\dot{V}_{75} (ml/sec)	$\Delta N_{2750-1250}$ (% × 100)
7–10 Years						
Lancaster (N = 68)	236 ^{±7†}	261 ^{±9}	269 ^{±16}	258 ^{±19}	125 ^{±13}	-7.9 ^{±1.7}
Long Beach (N = 29)	209 ^{±10}	216 ^{±15}	258 ^{±27}	232 ^{±25}	146 ^{±22}	+3.7 ^{±1.8}
11–14 Years						
Lancaster (N = 85)	124 ^{±9}	120 ^{±11}	147 ^{±17}	118 ^{±19}	98 ^{±13}	-1.7 ^{±1.2}
Long Beach (N = 24)	68 ^{±16}	75 ^{±22}	62 ^{±25}	41 ^{±23}	6 ^{±25}	+5.5 ^{±2.0}
15–18 Years						
Lancaster (N = 49)	11 ^{±7}	23 ^{±10}	-26 ^{±16}	-28 ^{±20}	-48 ^{±18}	-0.4 ^{±1.5}
Long Beach (N = 16)	-20 ^{±9}	-16 ^{±10}	-80 ^{±21}	-82 ^{±21}	-66 ^{±17}	+4.4 ^{±2.0}
19–24 Years						
Lancaster (N = 27)	-6 ^{±10}	-11 ^{±13}	-30 ^{±20}	-20 ^{±25}	-53 ^{±17}	-2.9 ^{±2.1}
Long Beach (N = 36)	-18 ^{±13}	-18 ^{±17}	-60 ^{±15}	-77 ^{±16}	-64 ^{±14}	+2.9 ^{±1.2}

*White, non-Spanish-surnamed only, had not changed job or residence because of a respiratory problem. FEV₁ exists at both times.

†Mean of annualized 5-year change; mean = (T2-T1/elapsed months × 12 ± standard error).

because of respiratory problems (2.1 percent in Long Beach and 0.5 percent in Lancaster).

A major way of assessing the impact of a lower-than-desired response rate is to determine the differences in the baseline test results between participants who were retested and those who were not. The difference in the mean test indices at baseline were not significantly different in those who were not retested than in those who subsequently completed lung function retesting, suggesting that those who were not retested were substantially similar in respiratory function to those who were.

A particular problem for cohort studies of the relationship of air pollution to changes in lung function test results is the possible impact of air pollution levels on the day of testing.⁸ For that reason, anal-

ysis was carried out comparing the results of lung function testing with levels of each of the major pollutants on the day of testing. No significant correlations with test results were seen and no consistent pattern emerged for the major pollutants occurring at higher concentrations in Long Beach, suggesting that the range of levels of these pollutants prevailing during the testing periods had relatively little impact on the results of the lung function testing in this study.

The tests used in this study can be affected by a number of confounding factors including instrument characteristics, subject effort, and technician performance.²⁹ Thus, there is continual concern with the accuracy and reliability of the equipment and testing procedures, particularly in a mobile laboratory in which movement of the equipment from site to

site can precipitate instrument drift. For that reason, the test-retest difference in FEV₁ observed in the five to six year interval in the Mobile Lung Function Laboratory was compared with results obtained on a 3 percent subsample of participants tested on both occasions at the UCLA Reference Laboratory. This comparison revealed only a small difference between the two laboratories in favor of showing a slightly greater deficit in FEV₁ in Long Beach if, in fact, the difference in deficit was also present in the entire group tested.

For the lung function tests, the mean of the absolute change in individual test results was used rather than differences in predicted values. Thus, differences between communities in age and height could have biased the results. The mean height was, however, similar in the two

TABLE 7—Magnitude of *t and Significance Levels for Differences in Rate of Change of Lung Function Test Results in Lancaster and Long Beach Participants with *p* < .05**

Sex/Age (years)		FEV ₁	FVC	FEF _{25-75%}	\dot{V}_{50}	\dot{V}_{75}	$\Delta N_{2750-1250}$
Males							
7-10	T=	—	—	—	—	—	-3.12
	P<	—	—	—	—	—	.002
11-14	T=	—	—	—	—	—	—
	P<	—	—	—	—	—	—
15-18	T=	—	—	—	—	—	-2.25
	P<	—	—	—	—	—	.03
19-24	T=	2.90	2.93	3.89	3.11	—	—
	P<	.006	.005	3×10^{-4}	.003	—	—
25-59	T=	2.15	2.74	2.55	1.97	—	-3.64
	P<	.032	.006	.011	.049	—	3×10^{-4}
Females							
7-10	T=	2.16	2.63	—	—	—	-4.85
	P<	.033	.001	—	—	—	1×10^{-8}
11-14	T=	2.87	—	2.52	2.04	3.33	-3.13
	P<	.005	—	.013	.044	.002	.002
15-18	T=	2.24	—	2.18	—	—	—
	P<	.023	—	0.33	—	—	—
19-24	T=	—	—	—	1.99	—	-2.66
	P<	—	—	—	.051	—	.01
25-59	T=	3.48	3.49	2.20	2.37	—	-6.20
	P<	5×10^{-4}	5×10^{-4}	.028	.018	—	1.6×10^{-9}

$$*t = \frac{\bar{X}_1 - \bar{X}_2}{S} \text{ where } S = \frac{S_1^2(N_1 - 1) + S_2^2(N_2 - 1)}{N_1 + N_2 - 2} \left(\frac{1}{N_1} + \frac{1}{N_2} \right)$$

areas. The mean ages of the two populations were similar although the females in Long Beach were on average three years older than females in Lancaster, whereas the males in Long Beach were on average one year younger than in Lancaster. A prior study of this population suggested that the rate of decline in FEV₁ remained fairly constant over the age range 25-59 years.³³

Recent reports have suggested that young individuals living in homes supplied with gas, especially for cooking, may have more respiratory problems than persons in homes that are supplied with electricity.³⁴⁻³⁸ The percentage of homes that used gas for heating, however, was exactly the same in both communities (94 percent).

Many people in Southern California commute long distances to workplaces in which they may experience air pollution patterns different from those at their place of residence. Individuals in Long Beach commuted to areas of lower levels of the major pollutants (except for oxidants), whereas most residents of Lancaster who commuted did so to areas of higher levels of pollution.²⁸ This pattern would tend to minimize the actual difference in pollutant exposures for participants in the two study

areas and, thus, would reduce the likelihood of observing a pollution effect on lung function test results.

A number of other factors that could have biased the results have been dealt with by restricting the population analyzed in this paper. Differences in racial distribution were reduced by including only White non-Spanish-surnamed participants in the analyses and by excluding individuals who reported a history of changing residence or occupation because of a respiratory problem at baseline. The number of individuals who had worked in an occupation that might be associated with respiratory injury was too high to permit excluding them from analysis. Their occupations were not concentrated in any one or two types of exposure and the duration of their employment in any type was generally less than five years. The proportion with such a history, however, was higher in Lancaster than in Long Beach and, thus, including them in the analysis probably reduced the likelihood of observing less favorable changes in Long Beach.

The average annual change in FEV₁ among these never-smoking adults was higher than has been reported in most previous population studies.^{6-8,39-41} The lev-

els observed in our study are comparable with some of the more recent reports of changes in lung function over time in occupational groups.⁴²⁻⁴⁴ Although we looked intensively for methodologic problems that may have caused these large rates of decline in adults, we were unable to identify any consistent factors that would account for the magnitude of decline observed in FEV₁. One possibility is that these large average annual declines in FEV₁ may reflect the accumulated respiratory effects of chronic exposure to air pollution. Supporting this hypothesis is the previous observation that the annual rate of decline in FEV₁ between 25 and 59 years of age in these populations increased only very slightly with age³³ in contrast to the significant increase in the annual rate of decline with aging reported in other publications.^{45,46} Because of local migration patterns, fewer of our older participants and more of our younger participants were raised in the Los Angeles area. This, and the consistently poorer (more positive) changes in $\Delta N_{2750-1250}$, even in the youngest participants in Long Beach, suggest that the younger members of our cohorts raised in Los Angeles may experience greater drops in their lung function test parameters when they reach later life

than the drop currently observed in the older members of our cohorts who were raised in less polluted areas. If in fact this hypothesis is true, it is cause for concern.

The test demonstrating differences most frequently and with the highest levels of significance was the $\Delta N_{2750-1250}$. Furthermore, in the youngest age groups this test often demonstrated the only significantly worse deterioration, suggesting that physiologic changes may be occurring in children that are not as readily identified by the presumably less sensitive spirometric tests until adulthood. Since the $\Delta N_{2750-1250}$ is thought to reflect function primarily in the small airways, the results of this cohort study suggest that this may be the site of earliest injury due to exposure to the type of air pollutants found in the Long Beach area. Buist and colleagues⁴⁷ and McCarthy, *et al.*,⁴⁸ have demonstrated that the single-breath nitrogen test is more sensitive than spirometry in detecting early functional abnormality involving the small airways. In cross-sectional studies we were not able to observe differences between communities in this parameter.^{27,28,30} We had previously observed, however, that the $\Delta N_{2750-1250}$ is subject to considerable variability which may account for the difficulty in identifying significant differences in cross-sectional studies.⁴⁹ Inter-subject variability may be a greater problem in cross-sectional studies than intra-subject variability in cohort studies in which differences in two measurements from the same individual are being considered.

Among adults who never smoked, rate of decline in all of the tests noted in Table 7 was significantly worse in residents of Long Beach except for the \dot{V}_{75} in which a directionally similar difference did not attain statistical significance.

Although the large differences in the results of $\Delta N_{2750-1250}$ in children in even the youngest age groups suggest that the small airways are the earliest site of pathology resulting from chronic exposure to the mix of air pollutants occurring in Long Beach, the greater deterioration in the spirometric indices indicates that by the time residents of the area reach adulthood, the adverse changes in the small airways have progressed and/or the large airways have become affected as well. It remains to be determined if the adverse changes in the lungs resulting from chronic exposure to this mix of pollutants causes sufficient respiratory impairment over a lifetime to reduce their ability to function satisfactorily or only reduces their considerable reserve

capacity without causing clinically significant functional impairment.

Ware, *et al.*, have studied the respiratory symptom and lung function effects of chronic exposure to TSP, SO₂, and TSO₄ at two different examinations one year apart in children 6–10 years of age in six cities in the United States and have found no relationship between respiratory parameters and levels of these pollutants.⁵⁰ While it is tempting to compare the results of that study to the present study there are several problems with doing so. First, the measures of air pollutants were different. Whereas Ware, *et al.*, used the mean of the 24-hour values, we used the means of the daily peak hourly values for SO₂, although for TSP and TSO₄ we used the 24-hour totals. Of greater importance is the fact that we looked at the mean annual change in lung function values within each individual over a five to six year interval whereas Ware, *et al.*, looked at the correlations of the pollutant values with FEV₁ and FVC at two time periods only one year apart. Thus, their study design was essentially two consecutive cross-sectional correlations to mean lung function values for groups of children in each area whereas we looked at the mean of change within each individual over a five-year period. Nonetheless, there are some similarities between the studies. Neither found consistent correlations between respiratory symptoms and levels of air pollutants. Further, we did not observe a significant correlation between change in lung function and pollutant level in males 7–10 years of age. The correlation we observed in both males and females 7–10 years was in the single-breath nitrogen test, a possibly more sensitive measure of early decrement in lung function. It will be interesting to observe whether Ware, *et al.*, find correlations between pollutant levels and lung function with additional follow-up of the children in these six cities. We did not consistently observe significant differences in FEV₁ and FVC in boys until 15–18 years. We did, however, observe consistent difference in earlier age groups using the single-breath nitrogen test.

We previously observed a greater deficit in several lung function test parameters between Lancaster and an area subject to very high levels of oxidants, Glendora.^{26,30} The greatest difference in pollutant exposures between Long Beach and Glendora was in the levels of oxidants (much higher in Glendora), nitrogen dioxide (higher in Long Beach), and SO₂ (higher in Long Beach). Mean levels of SO₄

were similar in these two communities and higher than in Lancaster which had primarily oxidant exposure, which, although high, was half that in Glendora. In the Long Beach comparison, the measures incorporating the large airways (FEV₁, FVC) were consistently significantly different in adults whereas only the FEV₁ in adult females in the Glendora comparison were significant. On the other hand, a significant difference in \dot{V}_{75} was observed only for Glendora. The deterioration in the single-breath nitrogen test in Glendora was significantly worse in every age-sex group under 25 years compared whereas they were significantly worse only in males 7–10 years and 15–18 years and in females 7–14 and 19–24 years in Long Beach. Significant differences in most of the spirometric indices in these younger age groups were not consistently identified in either polluted community compared to Lancaster. It is possible that the type of pollutants that were present in greatest concentrations in Long Beach (NO₂, hydrocarbons, and SO₂) were more likely to cause damage in the large airways whereas oxidants were more likely to cause damage in the smaller airways as reflected by the greater magnitude of differences for the $\Delta N_{2750-1250}$ and \dot{V}_{75} in Glendora. Further, exposure to oxidant pollutants may cause measurable damage earlier (according to the single-breath nitrogen test) than SO₂ and NO₂. These interpretations are consistent with results of controlled exposure studies in experimental animals which demonstrate that characteristic ozone-induced lesions occur in the lung periphery (centiacinar region)^{51,52} while chronic exposure to SO₂ produces clinical, physiologic, and histologic changes of chronic bronchitis with greater involvement of proximal than distal airways.⁵³

Given the nature of epidemiological studies which must deal with populations as they actually exist in the community rather than with laboratory animals which can be kept under experimental conditions, these inferences should be investigated further. It appears, however, that chronic exposure to either mix of pollutants results in less rapid growth of lung function in children and a greater rate of deterioration in adulthood.

These observations have serious implications for safeguarding the health of the public and controlling levels of pollutants in urban areas in the United States. These studies need to be verified by others, but the implications for health should not be ignored by legislators and govern-

ment administrators. Given the difficulties of carrying out epidemiologic studies of cohorts of individuals over long periods of time the probability of being able to observe statistically significant differences is smaller than for similarly designed studies done under laboratory conditions. For this reason, the burden of proof should now be to prove that high levels of these pollutants do not affect lung function and, therefore, until that is demonstrated efforts should be increased to improve the quality of air in the urban areas of the United States. □

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APPENDIX A

Single-breath Nitrogen Test

Ventilation distribution was determined using an Ohio-Series 700 nitrogen analyzer, Electro-Medical (Ohio Medical Products, Houston) model 780 spirometer, electronics module, sample-head assembly, remote vacuum pump assembly, and Hewlett-Packard X-Y recorder (Hewlett-Packard, San Diego) with time base.

Subjects performed these tests in the standing position with a nose clamp and flanged rubber mouthpiece in place. After a few normal tidal breaths and stabilization of the system, the subject was asked to exhale completely and to hold his breath briefly at the residual volume position. The valve was switched to the reservoir containing 100 percent oxygen and the expiratory port simultaneously opened to the (electronic) spirometer. The subject was asked to inhale fully and deeply, within less than 4 seconds, to total lung capacity, then to exhale slowly and completely at a constant flow rate maintained between 0.5 and 0.8l/s according to an X-Y tracing which was visible to him. Residual volume was reached over no longer than 10 s. The expired volume and expired nitrogen concentrations were simultaneously recorded on the horizontal and vertical axes of the X-Y recorder. A minimum of three trials was completed for each resident.

Each tracing was read by only one individual, the Chief Technologist, who assigned values for the percentage of nitrogen (percent N₂) in the expired air at 750 and 1,250 ml of expirate and identified both the point at which the inflection between phase III and Phase IV occurred and the point at which total volume was exhaled (residual volume).