# The Effect of Ambient Carbon Monoxide on Low Birth Weight among Children Born in Southern California between 1989 and 1993

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We evaluated the effect of carbon monoxide (CO) exposures during the last trimester of pregnancy on the frequency of low birth weight among neonates born 1989–1993 to women living in the Los Angeles, California, area. Using birth certificate data for that period, we assembled a retrospective cohort of infants whose mothers resided within 2 miles of 1 of 18 CO monitoring stations. Based on the gestational age and birth date of each child, we estimated last-trimester exposure by averaging the corresponding 3 months of daily CO concentrations registered at the monitoring station closest to the mother's residence (determined from the birth certificate). Where data were available (at 6 stations), we also averaged measurements taken daily for nitrogen dioxide and ozone and those taken at 6-day intervals for particulate matter ≤10 µm ($PM_{10}$) to approximate last-trimester exposures to other pollutants. Overall, the study cohort consisted of 125,573 singleton children, excluding infants born before 37 or after 44 weeks of gestation, those weighing below 1,000 or above 5,500 g at birth, those for whom fewer than 10 days of CO measurements were available during the last trimester, and those whose mothers suffered from hypertension, diabetes, or uterine bleeding during pregnancy. Within the cohort, 2,813 (2.2%) were low in birth weight (between 1,000 and 2,499 g). Exposure to higher levels of ambient CO (>5.5 ppm 3-month average) during the last trimester was associated with a significantly increased risk for low birth weight [odds ratio (OR) = 1.22; 95% confidence interval (CI), 1.03–1.44] after adjustment for potential confounders, including commuting habits in the monitoring area, sex of the child, level of prenatal care, and age, ethnicity, and education of the mother. *Key words:* air pollution, carbon monoxide, environmental hazard surveillance, epidemiology, health effects, low birth weight. *Environ Health Perspect* 107:17–25 (1999). [Online 7 December 1998]
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To date, few studies have investigated the effect of ambient air pollution on birth outcomes. Yet the human fetus is likely to be one of the populations most vulnerable to air pollutants. Numerous studies have demonstrated that maternal smoking during pregnancy increases the risk for delivering low birth weight (LBW), preterm, and small-for-gestational-age infants (SGA) (*1–5*). Moreover, environmental tobacco smoke—which elevates indoor levels of carbon monoxide (CO) and particulates ≤10 µm ($PM_{10}$)—is also associated with reduced birth weight and SGA (*6–12*). Such evidence is consistent with the hypothesis, first suggested over two decades ago, that ambient air pollutants, specifically CO, might have a deleterious effect on fetal growth and development (*13–15*).

The first study in a human population reporting a lower mean birth weight for babies whose mothers lived in areas of high air pollution was conducted in Los Angeles, California in the early 1970s (*16*). More recently, a study of Chinese women living in Beijing found elevated levels of sulfur dioxide ($SO_2$) and total suspended particles (TSP) to be associated with an increase in risk for delivery of low-weight (<2,500 g) full-term neonates (*17*). However, Wang et al. (*17*) had insufficient data to evaluate the influence of levels of CO or other air pollutants that might be correlated with the high TSP or $SO_2$ concentrations that were measured. No clear relationship was detected between average ambient levels of CO and low birth weight among babies born to Denver, Colorado, residents between 1975 and 1983 (*18*), perhaps reflecting the much lower ambient CO levels in Denver than those often found in the Los Angeles area.

In general, low birth weight is considered to be an important predictor of infant mortality and childhood morbidity, and may continue to be a risk factor for morbidity into adulthood (*19,20*). As Weinberg and Wilcox (*21*) have pointed out, however, low birth weight itself does not cause adverse health outcomes, but rather serves as a biomarker for the primary causal factors responsible for prenatal developmental disturbances that predispose to childhood disability. It is widely accepted that it is important to reduce exposure to risk factors for low birth weight whenever possible in order to decrease the associated burden of disability and disease. If birth weight is found to be sensitive to the toxic effects of air pollutants, it can be used as an easily monitored sentinel indicator for environmental hazard surveillance, available to any large population that routinely records birth information and ambient air pollution levels.

In our investigation of the influence of current levels of air pollutants on birth weight, we chose to concentrate on the effects of carbon monoxide because a biologic mechanism for fetal effects has been proposed for CO, but not for other air pollutants. Furthermore, studying the effect of CO requires an exposure assessment approach that differs from that suitable for other air pollutants because we cannot assume a homogeneous distribution of CO concentrations over large geographic areas. Finally, monitoring stations in the South Coast Air Quality Management District (SCAQMD) vary with respect to the range of pollutants monitored. Only 6 of 21 stations monitoring CO levels also measured all of the three other pollutants of interest [$PM_{10}$, ozone, and nitrogen dioxide ($NO_2$)] during the period of interest. Thus, the present study focuses on characterizing the effects of ambient CO levels on birth weight in the SCAQMD.

## Methods

***Exposure assessment.*** Between 1989 and 1993, monitoring data for ambient carbon monoxide levels were collected by the SCAQMD at 21 locations. Fixed-site monitors are most likely to reflect accurately only those ambient CO levels within a small perimeter of the station because CO levels are known to fall sharply with increasing distance from an emitting source (*22*). Staff at the SCAQMD therefore recommended that we extrapolate CO levels no farther than a 2-mile radius in order to avoid exposure misclassification (J. Cassmassi, personal communication). Thus, we restricted our study population to

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the infants of mothers residing within about 2 miles of a stationary air pollution monitor.

Previous studies in Denver and Los Angeles have demonstrated that stationary monitors provide a good measure of neighborhood CO exposure within a 1–2-mile radius (*23*). We chose the 2-mile radius criterion because the information about maternal residence that can be accessed from California birth certificates is restricted to zip codes, and the boundaries of the zip codes for our population fell outside a 1-mile radius in almost all instances. Indeed, 3 of the 21 SCAQMD stations with monitoring data for CO had to be excluded entirely, as the zip codes in their vicinity included large areas in excess of the 2-mile radius criterion. Thus, our analyses were based on 37 zipcode zones located largely within 2 miles of 1 of the 18 SCAQMD CO monitoring stations. Eleven of these zones lay entirely within 2 miles of a monitoring station; an additional 22 zones were situated such that more than 80% of their area fell within the 2-mile radius, and 4 more comprised areas that were 60–80% within the 2-mile range.

The staff of the SCAQMD recommended that we use for our analyses only those CO measurements taken from 0600 to 0900 hr, a period of lower wind speed in the Los Angeles basin, allowing for more reliable measurement of ambient CO levels. Accordingly, hourly measurements from the 0600–0900 period were averaged to estimate CO exposure in the vicinity of each of 18 monitoring stations. Six of these stations also provided air monitoring data for all three of the other pollutants of interest, including hourly round-the-clock measurements for $NO_2$ and ozone, as well as measurements at 6-day intervals for $PM_{10}$.

We limited our exposure assessments to the last trimester of gestation because the adverse effects of smoking, and thus potentially of air pollution, are mediated by chronic hypoxia during the last trimester; and in Western societies, birth weight is generally determined by factors impacting pregnancy after the 28th week of gestation (*24*). Furthermore, Wang et al. (*17*) showed that when modeling the effects of particulates and $SO_2$ on birth weight, third trimester averages best predicted the outcome.

***Subjects and outcome.*** Birth certificates, provided by the California Department of Health Services, were used to identify subjects, to determine third trimester dates (derived from gestational age at birth and birth date), and to ascertain birth weight and most covariates included in the analyses. Subjects were singletons born at term (between 37 and 44 weeks of gestation) to women living within zipcodes largely within 2 miles of a CO monitoring station.

In addition to eliminating multiple and premature births, we also excluded very low birth weight babies (<1,000 g; *n* = 43), very heavy babies (>5,500 g; *n* = 42), and the offspring of about 171 pregnancies for which it was noted on the birth certificate that the mother had suffered from uterine bleeding, hypertension, or diabetes prior to delivery. These exclusions were based on our assumption that any effect of ambient CO on such pregnancies would be far outweighed by the influence of the mothers' high-risk medical conditions and/or the treatments for those conditions. Additional analyses, however, showed that these exclusions did not alter our findings (results not shown). Further exclusion of study subjects was due to missing data for any of the variables included in our covariate-adjusted analyses, such as gestational age, birth

**Table 1.** Demographics (means and percentages) by air monitoring station district for 125,573 children born 1989–1993 in the South Coast Air Quality Management District

| | All stations | East San Gabriel Valley 1 | East San Fernando Valley | South coastal LA County | West San Fernando Valley | Pomona/ Walnut Valley 1 | Southeast LA County | South central LA County | South San Gabriel Valley |
|---|---|---|---|---|---|---|---|---|---|
| Number of births | 125,573 | 5,842 | 5,614 | 7,717 | 5,412 | 13,489 | 5,809 | 24,105 | 2,368 |
| Average last trimester CO exposures (ppm) | 2.59 | 1.44 | 2.93 | 2.16 | 2.37 | 2.75 | 2.31 | 3.72 | 2.49 |
| Mean birth weight (g) | 3,441.6 | 3,431.7 | 3,458.3 | 3,413.0 | 3,435.6 | 3,425.5 | 3,490.3 | 3,455.5 | 3,486.0 |
| Mean gestational age (days) | 280 | 280 | 280 | 280 | 281 | 280 | 281 | 281 | 281 |
| Mean age of mother (years) | 26.4 | 25.8 | 27.9 | 26.3 | 27.6 | 25.9 | 27.2 | 25.6 | 27.3 |
| Mean maternal education (years) | 10.8 | 10.8 | 12.3 | 11.5 | 11.7 | 10.3 | 12.5 | 9.5 | 12.6 |
| Low birth weight (%) | 2.24 | 2.28 | 1.82 | 2.62 | 1.94 | 2.41 | 1.89 | 2.37 | 1.86 |
| Received no prenatal care (%) | 1.37 | 0.87 | 0.36 | 2.03 | 0.65 | 1.36 | 0.46 | 1.82 | 0.76 |
| Received prenatal care after the first trimester (%) | 26.7 | 25.3 | 17.8 | 27.4 | 21.0 | 28.7 | 20.0 | 32.2 | 17.1 |
| Birth of a second and higher order child (%) | 57.9 | 60.3 | 53.5 | 58.5 | 54.6 | 62.0 | 56.8 | 61.6 | 52.9 |
| Maternal race (%) | | | | | | | | | |
| White | 82.7 | 90.3 | 84.7 | 59.5 | 84.9 | 82.6 | 88.5 | 88.6 | 90.2 |
| Hispanic among whites | 61.9 | 69.3 | 41.3 | 36.3 | 45.7 | 67.8 | 44.2 | 86.7 | 60.1 |
| Asian | 5.2 | 1.9 | 7.0 | 9.2 | 6.5 | 3.7 | 4.6 | 0.3 | 5.1 |
| African American | 8.9 | 4.3 | 3.2 | 22.0 | 4.1 | 11.5 | 2.6 | 10.1 | 1.7 |
| Maternal education (%) | | | | | | | | | |
| <9 years | 23.4 | 20.3 | 12.2 | 17.8 | 17.3 | 26.0 | 7.0 | 32.9 | 7.5 |
| 13–15 years | 15.4 | 17.3 | 20.5 | 19.1 | 20.5 | 14.3 | 25.8 | 8.9 | 22.6 |
| 16+ years | 11.6 | 6.9 | 21.8 | 15.8 | 17.0 | 7.2 | 15.4 | 2.2 | 18.9 |
| Maternal age (%) | | | | | | | | | |
| <20 years | 12.4 | 13.3 | 6.3 | 13.9 | 8.5 | 14.7 | 10.3 | 15.5 | 9.7 |
| >35 years | 10.0 | 7.3 | 13.0 | 10.7 | 11.8 | 8.7 | 9.8 | 8.2 | 11.7 |

weight, maternal age, infant sex, maternal race, prenatal care information, and maternal education ($n$ = 2,242). Finally, we required that more than 10 last-trimester CO measurements be available for each of the women whose infants were included, resulting in an additional 8,305 exclusions. It is worth noting that removing the data for all 10,803 excluded subjects did not significantly change any of the values of the variables used in our analyses (Table 1).

The outcome of interest was term low birth weight. It was analyzed as a dichotomous variable; thus, all subjects born weighing less than 2,500 g (but at least 1,000 g), were classified as low birth weight and compared to all those weighing in excess of 2,500 g at birth.

***Statistical methods.*** We grouped last-trimester averages for estimated neighborhood exposure to CO and other pollutants into percentiles of their distribution in the population (<50th, 50–95th, >95th percentile). Exposure to levels below the median was used as the reference category for each pollutant. The effect of ambient air pollution on low birth weight was evaluated through logistic regression analyses; a test for trend was performed using category midpoints as score values.

Several known risk factors for LBW that could potentially modify or confound the relationship with neighborhood CO levels were controlled in the logistic regression models. The most important predictor of birth weight is gestational age (measured in weeks), and we entered a linear and a quadratic term into the models to capture the leveling-off of the slope for weight gain during the last months of pregnancy. This approach was previously been described by Wang et al. (*17*). We adjusted for years of maternal age (<19, 20–29, 30–34, 35–39, >40), race (African American, White, Hispanic, Asian), years of education (0–8, 9–11, 12, 13–15, ≥16), parity (first birth vs. second or subsequent), interval since the previous live birth (≤12 months, >12 months), access to prenatal care (none, from first trimester, or later), and infant sex. We also conducted stratified analyses for maternal age, race, and education, as well as sex of the infant, to evaluate the consistency of the air pollution associations across strata, i.e., to identify any effect modification by these factors.

Risk factors for low birth weight that are not registered on California birth certificates include maternal active and passive smoking, pregnancy weight gain, marital status, birth weight of mother, and proportion of time spent at home versus at work or commuting. Employing census data, we were able to adjust to some extent for time commuting, which is of particular interest because CO levels can be extremely high inside cars. Drawing upon the 1990 census data for each zip code, we created several ecologic variables that reflect general differences across monitoring areas with respect to commuting habits. These variables included 1) the proportion of the working population in a zip-code area who spend more than 60 min commuting to work; 2) the proportion who walk to work; and 3) the proportion of employed women with children under 17 years of age. Only the first two variables remained in our final models when we employed the 10% change-in-effect criterion advocated by Greenland (*25*).

Furthermore, we restricted some of our analyses to the infants of women who had given birth to at least one earlier child. We assumed that women pregnant with a first

| Central Los Angeles | West San Gabriel Valley | Northwest coastal LA County | Southwest coastal LA County | Central Orange County | North Orange County | Saddle-back Valley | North coastal Orange County | Northwest San Bernardino Valley 2 | Central San Bernardino Valley 1 |
|---|---|---|---|---|---|---|---|---|---|
| 13,628 | 3,579 | 4,429 | 11,914 | 11,528 | 951 | 4,543 | 403 | 2,519 | 1,723 |
| 2.64 | 1.83 | 1.59 | 2.92 | 1.94 | 2.82 | 1.44 | 2.79 | 1.73 | 1.71 |
| 3,424.4 | 3,413.9 | 3,435.8 | 3,432.2 | 3,463.6 | 3,519.7 | 3,494.3 | 3,509.2 | 3,444.9 | 3,381.0 |
| 280 | 279 | 281 | 280 | 280 | 281 | 280 | 282 | 280 | 280 |
| 26.0 | 28.3 | 29.9 | 26.1 | 25.8 | 29.0 | 28.6 | 27.6 | 25.7 | 24.9 |
| 9.1 | 13.1 | 14.1 | 11.0 | 9.8 | 14.1 | 13.6 | 12.3 | 10.9 | 10.8 |
| 2.22 | 2.71 | 1.85 | 2.38 | 2.24 | 1.47 | 1.56 | 2.23 | 2.18 | 2.61 |
| 1.47 | 0.42 | 0.41 | 1.47 | 2.32 | 0.42 | 0.46 | 1.24 | 1.51 | 2.90 |
| 31.0 | 19.8 | 10.9 | 25.7 | 34.1 | 10.8 | 11.0 | 20.6 | 32.1 | 36.5 |
| 60.9 | 50.0 | 42.2 | 56.1 | 57.3 | 53.8 | 51.8 | 46.9 | 60.7 | 62.3 |
| 84.9 | 68.3 | 82.9 | 68.4 | 92.0 | 84.0 | 84.2 | 95.0 | 87.4 | 70.8 |
| 84.0 | 35.6 | 24.3 | 56.8 | 71.7 | 12.8 | 16.9 | 31.0 | 54.5 | 47.9 |
| 11.6 | 12.9 | 10.2 | 4.4 | 3.2 | 9.5 | 8.2 | 2.7 | 1.6 | 6.0 |
| 2.5 | 15.0 | 3.5 | 22.3 | 2.4 | 2.9 | 3.1 | 0.7 | 8.5 | 18.2 |
| 37.9 | 12.1 | 8.5 | 21.2 | 31.7 | 1.5 | 4.1 | 15.9 | 19.3 | 17.7 |
| 6.8 | 21.5 | 19.8 | 18.5 | 11.7 | 30.0 | 29.6 | 23.6 | 18.3 | 13.5 |
| 3.0 | 36.4 | 51.3 | 8.9 | 6.2 | 36.9 | 32.9 | 26.8 | 6.3 | 6.3 |
| 15.1 | 7.5 | 4.0 | 11.8 | 13.3 | 4.2 | 4.1 | 7.4 | 13.8 | 16.4 |
| 10.5 | 15.6 | 21.2 | 8.5 | 7.6 | 17.1 | 12.9 | 11.7 | 6.8 | 5.8 |

**Table 2.** Demographic differences among air-monitoring station districts according to the 1990 census

| | All stations | East San Gabriel Valley 1 | East San Fernando Valley | South coastal LA County | West San Fernando Valley | Pomona/ Walnut Valley 1 | Southeast LA County | South central LA County | South San Gabriel Valley |
|---|---|---|---|---|---|---|---|---|---|
| Working residents (%) | | | | | | | | | |
| Walk to work | 4.0 | 3.6 | 3.9 | 2.1 | 1.8 | 2.7 | 1.8 | 3.3 | 1.3 |
| Drive a car to work | 85.2 | 89.6 | 88.3 | 86.6 | 89.1 | 90.3 | 93.9 | 86.8 | 93.7 |
| Ride a bus to work | 7.0 | 2.6 | 4.4 | 7.8 | 5.3 | 2.8 | 1.4 | 6.9 | 2.3 |
| Travel >60 min | 8.1 | 10.0 | 5.2 | 6.6 | 9.0 | 13.0 | 7.9 | 8.0 | 7.4 |
| Working women among women with children[a] (%) | | | | | | | | | |
| With children 1–17 years of age | 54.2 | 58.0 | 60.4 | 54.3 | 60.1 | 52.3 | 64.9 | 44.8 | 66.1 |
| With children ≤5 years of age | 26.8 | 31.5 | 25.5 | 26.1 | 28.8 | 28.1 | 28.2 | 22.6 | 32.3 |
| Working women among all women without children[a] (%) | 49.2 | 52.0 | 54.6 | 49.0 | 54.4 | 47.8 | 54.4 | 40.3 | 54.5 |
| Employed mothers of children ≤5years of age among single mothers (%) | 52.3 | 47.8 | 60.9 | 40.7 | 71.0 | 48.6 | 59.9 | 45.2 | 64.8 |
| Employed mothers of children ≤5 years of age among married mothers (%) | 51.7 | 60.6 | 52.8 | 48.5 | 55.1 | 51.6 | 58.1 | 45.4 | 59.2 |
| Families living below the poverty limit with children ages 1–17 among all families (%) | 12.2 | 8.7 | 7.4 | 14.5 | 5.1 | 11.7 | 3.3 | 16.3 | 4.6 |

[a]Age >15 years.

**Table 3.** Last-trimester averages (ranges) and Pearson-correlation coefficients for 4 pollutants and 48,021 births occurring in 2-mile radii of six monitoring stations in the SCAQMD between 1989 and 1993

| | | Pearson-correlation coefficients | | |
|---|---|---|---|---|
| Pollutant | Last trimester average (range) | CO | $NO_2$ | $PM_{10}$ |
| CO (ppm) | 2.45 (0.65–6.70) | 1.0 | | |
| $NO_2$ (pphm) | 4.12 (1.22–7.42) | 0.62 | 1.0 | |
| $PM_{10}$ (μg/m$^3$) | 48.0 (18.38–90.17) | 0.39 | 0.73 | 1.0 |
| Ozone (pphm) | 2.09 ( 0.30–4.94) | -0.65 | -0.47 | -0.10 |

Abbreviations: SCAQMD, South Coast Air Quality Management District; $PM_{10}$, respirable particulate matter ≤10 μm; pphm, parts per hundred million.

child might work up to the time of birth, while women with other children at home would be more likely to choose not to work or to work in closer proximity to their home during pregnancy. This supposition is supported by census data indicating that women with small children are less likely to be employed than those with no children or with older children only (see Table 2). We also restricted some analyses to young mothers (<20 years of age) who might be expected to spend their pregnancy in close proximity to their homes and schools.

As an additional approach to separating the effect of ambient CO exposure from that of other risk factors for LBW that vary across monitoring areas, we conducted further analyses focusing exclusively on the residents living in proximity to the one monitoring station for which the largest range of average CO levels were recorded during the study period. Between 1989 and 1993, approximately 24,000 children were born to women living within a 2-mile radius of this station. To increase the sample size, we also explored the effect of expanding the 2-mile radius to a 5-mile radius when calculating last-trimester averages for this one station.

## Results

The mean birth weight of all 125,573 (out of 136,376 eligible) children included in our analyses was 3,442 g. Of this total, 2,813 (2.24%) were classified as term LBW (1,000–<2,500 g). Within the "multipollutants" subcohort, which included only infants for whom we were able to obtain measurements for all four pollutants, plus all the confounding variables, there were 46,921 normal weight and 1,100 (2.29%) LBW term children.

The distribution of births and the known predictors of LBW by monitoring area are shown in Table 1. There were distinct differences from one location to the next with respect to racial composition, mean educational level, and socioeconomic status. The differences in socioeconomic status were evident both in birth certificate data, which indicated the percentage of women who did not receive prenatal care, and in census data, which specified the percentage of women who had children and whose income fell below the poverty limit.

Pearson correlations of last-trimester averages for the four pollutants of interest showed that CO was moderately correlated with $NO_2$ (Table 3). This relationship was expected because a large percentage of both pollutants are produced by the same vehicular sources. On the other hand, CO levels were negatively correlated with ozone levels, a reflection of the pattern of winter highs for CO and summer highs for ozone.

After adjustment for all confounding factors available on birth certificates as well as for differences in commuting habits across areas of monitoring (see Table 4), we found a 22% increase in LBW [odds ratio (OR) = 1.22; 95% confidence interval (CI), 1.03–1.44] among the children born to mothers who were exposed on average to more than 5.5 ppm CO (95th percentile for exposure) during the last trimester of pregnancy (Table 5). The excess of LBW infants rose to 33% for mothers giving birth to a second or higher order child and to 54% for mothers under the age of 20 years. However, for the latter groups, the confidence intervals

| Central Los Angeles | West San Gabriel Valley | Northwest coastal LA County | Southwest coastal LA County | Central Orange County | North Orange County | Saddle-back Valley | North coastal Orange County | Northwest San Bernardino Valley 2 | Central San Bernardino Valley 1 |
|---|---|---|---|---|---|---|---|---|---|
| 9.2 | 9.3 | 8.2 | 3.3 | 4.0 | 1.3 | 1.0 | 3.0 | 2.2 | 4.5 |
| 65.4 | 81.1 | 77.9 | 86.3 | 84.2 | 93.2 | 93.3 | 86.9 | 91.4 | 85.6 |
| 22.0 | 4.4 | 7.4 | 7.1 | 6.6 | 1.4 | 0.8 | 4.2 | 1.8 | 3.3 |
| 8.1 | 6.8 | 2.9 | 5.8 | 6.7 | 10.9 | 9.4 | 5.9 | 12.9 | 6.3 |
| 42.2 | 57.4 | 60.6 | 58.1 | 62.8 | 62.4 | 66.1 | 62.1 | 54.8 | 41.8 |
| 19.6 | 31.8 | 25.9 | 29.2 | 34.6 | 21.4 | 29.5 | 33.2 | 25.7 | 23.1 |
| 40.2 | 56.0 | 59.4 | 53.4 | 55.1 | 43.5 | 64.9 | 67.1 | 48.6 | 38.1 |
| 40.7 | 65.4 | 71.3 | 55.6 | 51.1 | 88.1 | 79.8 | 73.9 | 43.2 | 32.6 |
| 41.4 | 55.7 | 53.5 | 53.3 | 64.0 | 47.3 | 56.9 | 53.5 | 51.6 | 39.1 |
| 25.6 | 6.7 | 2.1 | 12.2 | 9.3 | 0.7 | 1.2 | 5.8 | 11.8 | 26.1 |

**Table 4.** Odds ratios (ORs) and 95% confidence intervals (CIs) for low birth weight by all covariates included in the adjusted model (see Table 5), including all eligible births that occurred between 1989 and1993; *n* = 125,573

| Covariate | OR | (CI) |
|---|---|---|
| Gestational week | 0.001 | (0.000–0.002) |
| Gestational week squared | 1.09 | (1.08–1.10) |
| Female child | 1.50 | (1.39–1.62) |
| Maternal race | | |
| White (reference) | 1.0 | |
| African American | 2.19 | (1.94–2.47) |
| Asian | 1.27 | (1.06–1.51) |
| Hispanic among whites | 0.87 | (0.78–0.97) |
| Maternal age (years) | | |
| 20–29 (reference) | 1.0 | |
| ≤19 | 0.87 | (0.77–0.98) |
| 30–34 | 1.14 | (1.03–1.27) |
| 35–39 | 1.40 | (1.22–1.62) |
| ≥40 | 1.23 | (0.91–1.67) |
| Maternal education (years) | | |
| 12 (reference) | 1.0 | |
| 0–8 | 0.99 | (0.88–1.17) |
| 9–11 | 1.16 | (1.04–1.30) |
| 13–15 | 0.77 | (0.68–0.87) |
| ≥16 years | 0.65 | (0.56–0.76) |
| Prenatal care received | | |
| In first trimester (reference) | 1.0 | |
| After the first trimester | 1.34 | (1.23–1.46) |
| None | 2.74 | (2.21–3.40) |
| Time since last live birth >12 months | 0.59 | (0.55–0.65) |
| Percentage of population (census) | | |
| Travel time to work >60 min | 5.57 | (1.16–26.8) |
| Walking to work | 5.64 | (2.02–15.7) |

around the effect estimate were wide; i.e., there was less statistical precision due to the decreasing size of the cohort. Among the offspring of women exposed to CO in the 50–95th-percentile range, the odds of LBW were considerably smaller, just 2–4% higher than for infants whose mothers' exposure to CO fell below the median level.

We applied the same types of analyses to that subset of the cohort for which multipollutant exposure data were available, enabling us to correct for the influence of non-CO pollutants (Table 6). The effects of CO appeared more pronounced after adjustment for concurrent exposures to $NO_2$, $PM_{10}$, and ozone (OR = 1.38 for CO exposures above 5.5 ppm; CI, 0.86–2.22). At CO levels of 2.2–5.5 ppm (50–95th percentile for exposure), the effects, although modest, increased enough after the multipollutant adjustment to suggest a dose–response effect of CO on LBW. However, the 95% confidence intervals for all of these subcohort analyses were wide and spanned the null value, again because statistical precision declined with the decreasing size of the study population.

Focusing on the monitoring station reporting the largest range of CO levels (South central Los Angeles County), we

**Table 5.** Odds ratios (ORs) and 95% confidence intervals (CIs) for low birth weight by last-trimester ambient CO levels in 1989–1993, measured at 18 stations[a,b]

| | All children living in a 2-mile radius of a monitoring station (case, *n* = 2,809; noncase, *n* = 122,764) | | Higher parity children only (case, *n* = 1,454; noncase, *n* = 73,687) | | Women younger than 20 years of age[c] (case, *n* = 420; noncase, *n* = 15,111) | |
|---|---|---|---|---|---|---|
| CO level (ppm) | Crude OR (CI) | Adjusted OR (CI) | Crude OR (CI) | Adjusted OR (CI) | Crude OR (CI) | Adjusted OR (CI) |
| <2.2[d] | 1.0[e] | 1.0[e] | 1.0[e] | 1.0[e] | 1.0[e] | 1.0[e] |
| 2.2 – <5.5[f] | 1.08 (1.00–1.16) | 1.04 (0.96–1.13) | 1.07 (0.96–1.19) | 1.03 (0.92–1.15) | 1.03 (0.84–1.26) | 1.02 (0.83–1.26) |
| ≥5.5[g] | 1.32 (1.12–1.55) | 1.22 (1.03–1.44) | 1.47 (1.19–1.81) | 1.33 (1.07–1.65) | 1.64 (1.15–2.35) | 1.54 (1.07–2.22) |

[a] Adjusted for gestational week, gestational week squared, female child, maternal race (African American, Asian, Hispanic), maternal education (0–8, 9–11, 12, 13–15, >16 years), maternal age (<19, 20–29, 30–34, 35–39, >40 years), no prenatal care, prenatal care received after first trimester, last live birth >12 months, travel time to work >60 min (census), and walking to work (census).

[b] Excluded are children of mothers with pregnancy complications, birth weights <1,000 g and >5,500 g, and all children with missing values for one of the variables included in the adjusted models.

[c] Model does not include education of mothers >12 years.

[d] ≤50th percentile for last trimester CO averages for 125,573 children.

[e] Reference category.

[f] 50–95th percentile for last trimester CO averages for 125,573 children.

[g] ≥95th percentile for last trimester CO averages for 125,573 children.

**Table 6.** Odds ratios (ORs) and 95% confidence intervals (CIs) for low birth weight by last-trimester ambient CO levels measured at six stations that monitored all four pollutants[a,b]

| CO level (ppm) | All children living in a 2-mile radius of a monitoring station (case, *n* = 1,100; noncase, *n* = 46,921) |  | Higher parity children only (case, *n* = 584; noncase, *n* = 28,313) |  | Women younger than 20 years of age[c] (case, *n* = 146; noncase, *n* = 5,918) |  |
|---|---|---|---|---|---|---|
|  | Crude OR (CI) | Adjusted OR (CI) | Crude OR (CI) | Adjusted OR (CI) | Crude OR (CI) | Adjusted OR (CI) |
| <2.2[d] | 1.0[e] | 1.0[e] | 1.0[e] | 1.0[e] | 1.0[e] | 1.0[e] |
| 2.2–<5.5[f] | 1.06 (0.94–1.19) | 1.10 (0.91–1.32) | 1.08 (0.92–1.27) | 1.24 (0.96–1.60) | 1.02 (0.73–1.42) | 1.30 (0.77–2.20) |
| ≥ 5.5[g] | 1.32 (0.88–1.98) | 1.38 (0.86–2.22) | 1.48 (0.86–2.56) | 1.92 (1.02–3.62) | 3.28 (1.47–7.33) | 5.08 (1.77–14.63) |

[a] Adjusted for gestational week, gestational week squared, female child, maternal race (African American, Asian, Hispanic), maternal education (0–8, 9–11, 12, 13–15, ≥16 years), maternal age (≤19, 20–29, 30–34, 35–39, ≥40 years), no prenatal care, prenatal care received after first trimester, last live birth >12 months, travel time to work >60 min (census), and walking to work (census), $NO_2$, $PM_{10}$, and ozone (each pollutant in four categories representing the <50th, 50–75th,75–95th, ≥95th percentiles).

[b] Excluded are children of mothers with pregnancy complications, birth weights <1,000 g and >5,500 g, and all children with missing values for one of the variables included in the adjusted models.

[c] Model does not include maternal education >12 years.

[d] ≤50th percentile for last trimester CO averages for 125,573 children.

[e] Reference category.

[f] 50–95th percentile for last trimester CO averages for 125,573 children.

[g] ≥95th percentile for last trimester CO averages for 125,573 children.

**Table 7.** Adjusted odds ratios (ORs) and 95% confidence intervals for low birth weight by last-trimester ambient CO levels measured at the South Central Los Angeles station only (2-mile radius: case, *n* = 572; noncase, *n* = 23,533; 5 mile radius: case, *n* = 2,805; noncase, *n* = 94,160)[a,b]

| CO level (ppm) | First trimester (2-mile radius) | Second trimester (2-mile radius) | All trimesters (2-mile radius) | Third trimester (2-mile radius) | Third trimester (5-mile radius) |
|---|---|---|---|---|---|
| <50th percentile[c] | 1.0[d] | 1.0[d] | 1.0[d] | 1.0[d] | 1.0[d] |
| 50–95th percentile[e] | 0.87 (0.73–1.03) | 1.02 (0.85–1.20) | 0.99 (0.83–1.18) | 1.06 (0.89–1.26) | 1.07 (0.99–1.16) |
| ≥95th percentile[f] | 0.82 (0.54–1.24) | 0.97 (0.65–1.44) | 0.86 (0.60–1.23) | 1.24 (0.87–1.77) | 1.24 (1.06–1.45) |

[a] Adjusted for gestational week, gestational week squared, female child, maternal race (African American, Asian, Hispanic), maternal education (0–8, 9–11, 12, 13–15, ≥16 years), maternal age (≤19, 20–29, 30–34, 35–39, ≥40 years), no prenatal care, prenatal care received after first trimester, and last live birth >12 months.

[b] Excluded are children of mothers with pregnancy complications, birth weights <1,000 g and >5,500 g, and all children with missing values for one of the variables included in the adjusted models.

[c] First trimester <3.6 ppm, second trimester <3.4 pm, third trimester <3.7 ppm, all trimesters <3.7 ppm.

[d] Reference category.

[e] First trimester <3.6–7.2 ppm, second trimester 3.4–7.0 ppm, third trimester 3.7–7.0 ppm, all trimesters 3.7–4.9 ppm.

[f] First trimester >7.2 ppm, second trimester >7.0 ppm, third trimester >7.0 ppm, all trimesters >4.9 ppm.

found results that were similar to those obtained for all stations combined whether we used a 2-mile or a 5-mile radius from the CO monitor as our cut-off for the study population for that station (OR = 1.24 for CO exposures above the 95th percentile; see Table 7). When using first- or second- or all-trimester averages instead of third-trimester averages as our measure of exposure, we found no effect for CO on LBW, as predicted for children born in a Western society.

## Discussion

The biological mechanisms whereby air pollution might influence birth weight remain to be determined. Nevertheless, it is known that CO crosses the placental barrier and that the hemoglobin in fetal blood has 10 times more affinity for binding CO than does adult hemoglobin. Moreover, some animal studies have indicated that fetal growth might be retarded by the direct toxic effects of CO and/or nicotine and other substances generated by burning cigarettes (*26*).

In the early 1970s, a study of 533 nonsmoking women who all delivered in the same maternity hospital in Los Angeles reported a lower mean birth weight for babies of mothers who lived in areas of higher air pollution. When the measures of air pollution exposure consisting of CO, $NO_2$, and ozone levels recorded at the monitoring station nearest to a woman's residence were averaged over the entire pregnancy, only CO levels were statistically significantly linked to decreased birth weight. Trimester-specific results, however, showed that increased levels of all three pollutants contributed to lower birth weight. The decrement of 314 g in mean weight for infants born in heavily polluted versus lightly polluted areas was as large as the difference expected for the offspring of women who smoke a pack of cigarettes per day during pregnancy. This result is less surprising in light of the levels of ambient CO pollutants in the early 1970s, which routinely exceeded 300 ppm in the Los Angeles basin. Such high concentrations could produce increases in blood carboxyhemoglobin (to 6–10% of total hemoglobin) equal to those observed in persons smoking one pack of cigarettes a day (*27*).

Only one other published American study has examined the effect of ambient CO on birth weight. This investigation found no clear relationship between ambient levels of CO averaged over the last trimester of pregnancy and LBW in the Denver population (*18*). The study included all infants born low in weight (*n* = 998) between 1975 and 1983 and compared them with a sample of normal birth weight babies (*n* = 1,872). Last-trimester average exposure to CO was calculated from the levels measured at an air monitor located within a 2-mile radius of the census tract in which the mother resided.

The CO levels reported for Denver during the study period (median ranged from 0.5 to 3.6 ppm) were considerably lower than those seen in Los Angeles during the 1970s and, indeed, did not reach the higher concentrations still frequently encountered in Los Angeles in the 1990s. Moreover, in laboratory studies in which rabbits were exposed to controlled amounts of CO throughout gestation, low birth weight was seen only at levels of 90 ppm or greater (*28*), greatly exceeding the averages in Denver. Nevertheless, in the subgroup of Denver census tracts judged to reflect most accurately the ambient levels of CO, Alderman et al. (*18*) found a small but nonsignificant increase in LBW for average CO exposures ≥3 ppm (OR = 1.5; CI, 0.7–3.5). This observation suggests that there might be an effect of low levels of ambient CO that could not be detected definitively in the Denver study because of the relatively small study size.

Recently, a group of researchers examined the effect of ambient air pollutants on birth weight among Chinese women delivering their first child in Beijing in 1988 (*17,29*). These authors found dose–response relationships between third-trimester exposure to $SO_2$ and TSP and the birth weight of term babies. Thus, the risk of giving birth to a low weight baby was increased by 11% for each 100 µg/$m^3$ increase in $SO_2$ (OR = 1.11; CI, 1.06–1.16) and about 10% for each 100 µg/$m^3$ increase in TSP (OR = 1.10; CI, 1.05–1.14). These significant increases in risk for low birth weight were evident despite analyses indicating that absolute birth weight was reduced by only 7.3 and 6.9 g for each 100 µg/$m^3$ increase in $SO_2$ and TSP, respectively. Wang et al. (*17*) suggested that pregnancies at high risk for low birth weight might be particularly susceptible to the adverse effects of air pollutants. The question of whether the pollutants responsible for the observed effects were $SO_2$ and TSP, however, could not be resolved by this study. Only $SO_2$ and TSP were measured at the Beijing monitoring stations. Yet, the levels of those compounds may have served primarily as proxy measures for other pollutants concomitantly released from the same sources (mainly the burning of coal for heating and cooking).

Our study found that of all the pollutants measured in the Los Angeles area, ambient CO was the most consistent and important predictor of LBW in term infants. We did not look for shifts in absolute mean birth weight to gauge whether CO might affect all births and not just those near the lower end of the weight spectrum. Although pollution-related shifts in overall birth weight were observed in the Beijing study (*17*), they were quite small. Shifts of similar magnitude could easily be obscured in the Los Angeles cohort, which was considerably more heterogeneous than its Beijing counterpart with respect to such factors as maternal smoking, access to health care, and sources of pollution. We therefore focused on low birth weight as the more sensitive indicator of environmental effects, reflecting the vulnerability of a high-risk population. Thus, rather than testing for a displacement of the whole birth weight distribution, we determined whether CO exposure affected the spread in the lower tail of the distribution.

As was done in the Beijing study (*17*), we restricted our evaluation to full-term live births (gestational age 37–44 weeks) in order to assess whether ambient pollutant levels could retard intrauterine growth. This limitation was important because preterm births, while commonly characterized by low birth weight (<2,500 g), result from quite different pathophysiological processes than those causing intrauterine growth retardation and might also lead to different neonatal and postneonatal complications (*30–32*). We included gestational age (in weeks) as well as the square of gestational age in all of our models. The regression coefficients therefore can be interpreted as the effect of CO on gestational age-specific birth weight.

Although our analyses controlled for a number of potential confounders, we did not have the information to adjust for some known risk factors for low birth weight. Most important, the records available to us did not have any indication of maternal nutrition or prepregnancy weight, history of adverse pregnancy outcomes, occupational exposures, or smoking experience. We also did not have the benefit of being able to draw upon a relatively homogeneous population of mothers with few or no smokers, an advantage of both the Beijing (*17*) and the 1970s Los Angeles (*16*) studies. On the other hand, when we restricted our analyses to residents living near the one monitoring station recording the largest range of average CO levels (south central Los Angeles station), we found an adjusted OR of 1.24 for the effect of >7.0 ppm (95th percentile) CO on LBW (Table 7), similar to the effect observed for residents of all monitoring areas combined. Thus, given that the population living in a 2-mile radius of a single station is much more homogeneous with respect to social, economic, and behavioral risk factors than the total population under investigation, it appears unlikely that our effect estimates would be attributable only to variations in the distribution of those factors between monitoring stations.

Furthermore, we were able to adjust for almost all risk factors considered previously as confounders in the Denver study. Because those adjustments accounted for maternal age, race, and education—factors that the National Center for Health Statistics has identified as influencing the smoking behavior of pregnant women—we may have indirectly adjusted for smoking in our study. Moreover, even the risk factors for which we had no information would be likely to vary independently of the average ambient CO levels encountered during the last trimester of pregnancy and so should not confound the relationships we observed with CO.

Thus, ambient CO levels for most of the Los Angeles monitoring stations followed a distinct pattern of winter highs and summer lows (with different ranges) unlikely to be correlated with most potential confounders. This seasonal fluctuation in ambient CO levels was related to the increase in CO emissions per mile for vehicles driven in cold weather and seasonal variations in average wind speed that affect dilution and dispersion of emissions, with low temperatures reducing surface vertical mixing and causing near-surface inversions to be stronger and last longer (*33*). Confounding by a risk factor such as smoking, then, could not occur unless women living in a given district tended to smoke more in the last trimester during periods when ambient CO levels happened to be elevated in that area, especially in winter. Further evidence that confounding in our study was likely to be minimal can be seen in Tables 5 and 6, which show that adding to our models all the potential confounders for which we had information did not appreciably change our estimates for the effect of CO on LBW.

The most important source of bias in our study is due to misclassification of exposure. Our estimates of individual exposures to CO during the last trimester were based on average measures of ambient CO for entire air monitoring districts. Yet, determinants of individual exposure are numerous, and accurate prediction of individual dose levels would require taking a myriad of microenvironments into account (*23*). In our cohort, the main factors expected to contribute to differences between area-wide and individual exposures are as follows.

First, CO levels might vary locally, even within a 2-mile radius of the same monitoring station, such that pregnant women living close to a major roadway or other CO source might be more heavily exposed than those living farther away. The extent of such misclassification could be assessed only through the use of exact address information that was not available to us. With such information it would be possible to apply modeling techniques to predict how exposure might vary depending on proximity of the residence to CO sources such as roadways and to the monitoring station itself.

Second, indoor sources of CO, while undetectable by the ambient-air monitoring stations, may add significantly to the overall burden of exposure for some individuals. The most important indoor sources of CO are generally gas- and wood-burning stoves and second-hand cigarette smoke (*34*). Building volume, ventilation rates, and proximity to a garage also influence indoor CO levels. However, outdoor levels of CO determine a large percentage of the indoor levels if no indoor sources exist (*21*), as may often be the case in the relatively warm climate typical of the Southern California area. Furthermore, although adult Southern Californians spend about 94% of their time indoors (*35*), residential air exchange rates are higher in the Los Angeles region than in the rest of California and the United States, presumably because people in Los Angeles leave windows and doors open more often (greatest air exchange rates are reported at temperatures of 66–70°F) (*36*).

Finally, the mothers of our cohort may have spent substantial amounts of time outside the perimeter of the monitoring district during the last trimester of pregnancy, while working, for example. Moreover, those who worked outside the area may have been exposed to high levels of CO inside vehicles in the course of commuting (*37*). We were able to adjust to some extent for the latter possibility by including measures of area-wide commuting habits in our analyses.

Although it was not feasible to obtain personal information about all CO exposures for each individual in our study, the question remains whether the incremental CO not captured by ambient air monitors was distributed differentially between the groups with high and low measures of third-trimester exposure to ambient CO. Only if there were such a correlation between the undetected CO exposures and those registered by the monitors would there be a biasing of our estimates for the effect of ambient CO away from the null (thus inflating the observed odds ratios). Evidence that personal air pollution exposures missed by fixed-site air monitors are not differentially distributed was provided by a 1995 study (*38*); when area-wide measures of exposure to air pollution, such as those obtained from fixed-site monitoring, were used as a proxy for personal exposures, the resulting estimates of pollutant effects were smaller (biased toward the null) than those based on the true exposures determined by personal sampling. Other authors have reported similar findings (*39,40*), demonstrating that nondifferential exposure misclassification can be reduced by supplementing ambient air-monitoring data with human time–activity pattern information, a refinement that has resulted in increased estimates for the effects of the air pollutants studied.

An indication that nondifferential exposure misclassification may have led to an underestimation of ambient CO effects in our study can be seen in our effect-modification evaluations. Subgroup analyses for determining whether the effects of CO were influenced by maternal age, race, education, or infant sex showed little variation across strata, with one exception. The offspring of very young women (<20 years of age) appeared to be consistently more strongly affected by ambient CO levels than the infants of older mothers (see Tables 5 and 6). We interpret these elevated effect estimates for the infants of younger women as a sign of reduced nondifferential misclassification bias in this maternal-age group compared to the others. Since pregnant teenagers are less likely than others to work far from home and more likely to attend a local school, their personal CO exposures may come closest to the levels measured by the nearest ambient monitor, so that one could expect the effects of CO in this subgroup to be less obscured by errors in exposure classification. However, we cannot exclude the possibility that some of the increment in the odds ratios for infants born to very young women may reflect an increased vulnerability to pollutants due to physical immaturity in the mother or due to other risk factors.

Recommendations have frequently been made to reduce exposure misclassification errors by using personal monitoring equipment to collect higher quality exposure data. However, this recommendation needs to be viewed within the context of the constraints inherent in environmental epidemiologic studies. Environmental exposures are typically considerably lower than those studied in occupational settings, so that large populations are often required to detect effects, a problem compounded when the outcomes of interest are rare. The costs of personal monitoring in large populations can be prohibitive. Moreover, while workers may be required to wear personal monitors, it is doubtful that it would be easy to obtain cooperation from a large population of pregnant women, even if cost were no object.

It was the availability of preexisting exposure records from local pollution-monitoring stations that allowed us to study a population of over 100,000, giving us a great advantage in enhanced statistical power to detect small effects at low levels of exposure. Furthermore, although we did not have personal monitoring data, we were able to calculate averages for exposure to ambient air pollutants specific to the last trimester for each individual pregnancy. Finally, because we relied on data that is continuously and routinely collected by public agencies, our work can easily be replicated at different times and in other populations.

We believe that the most efficient and cost-effective strategy for evaluating pollution-related effects is first to screen large populations broadly using existing ambient-monitoring records, as we have done in the present study. Once an exposure–outcome association has been established, in-depth assessments can be conducted on a subset of individuals with the outcome of interest (e.g., mothers who have given birth to term low birth weight babies), matching them with controls and interviewing each to collect the personal information needed to evaluate the influence of factors such as occupation, time spent in the area of residency, time commuting, nutrition during pregnancy, and indoor sources of pollution. This information, combined with a small validation study of exposure assessment via personal monitors, should serve to refine our understanding of pollutant effects and interactions, resolving many of the questions and uncertainties that could not be addressed in the broader screening study.

Through such follow-up of the present cohort, we plan to examine a number of CO sources in addition to those detected by ambient monitoring to determine how much each type of exposure contributes to low birth weight. Also, still to be addressed is the question of whether elevated ambient CO levels are more or less harmful in mothers who are concurrently exposed to CO from smoking, commuting, or other sources. Further studies should track the effects of CO throughout the gestational period to identify the peak period(s) of sensitivity for a range of possible adverse outcomes, including spontaneous abortion, fetal death, birth defects, and prematurity.

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