Effect of Carbon Black Exposure on Respiratory Function and Symptoms

Philip Harber, MD, MPH
Henry Muranko, MPH, CIH
Sofia Solis, BA
Ani Torossian, BS
Brenda Merz, MPH

Carbon black is a widely used pigment and filler. Some, but not all, previous studies have suggested an effect of long-term exposure upon the lungs. Carbon black production facility employees (1755) participated in the third round of the industry-wide medical surveillance testing. They were employed in 22 North American plants. Spirometry and a systematically administered questionnaire were included in the year 2000 round of the industry-wide medical surveillance program. Industrial hygiene data from an industry-wide survey in 2000–2001, as well as all available exposure assessment data collected since 1979, were integrated with process questionnaires and exposure rating questionnaires completed by plant personnel. Analyses included multiple linear regression and categorical data analyses. Multiple regression analyses showed statistically significant, consistent relationships between cumulative exposure and small reductions in forced expiratory volume in 1 second (FEV_1) but not with other spirometry parameters. The estimated slopes were -2 mL FEV_1 per mg-year/m^3 of cumulative 'total' dust exposure and -0.7 mL FEV_1 per mg-year/m^3 of cumulative exposure for the inhalable fraction. In addition, heavy cumulative exposures were associated with a small increase in chronic bronchitis in nonsmokers. Recent exposures, typically much lower than in the past, were not demonstrated to be associated with these effects. Consistent with good occupational hygiene practice for any contaminant, workplace exposures to carbon black should be controlled to lowest practical levels. (J Occup Environ Med. *2003;45:144–155*)

From the Division of Occupational and Environmental Medicine, Department of Family Medicine, University Of California, Los Angeles (Dr Harber, Ms Solis, Ms Torossian, Ms Merz) and Muranko & Associates, Scottsdale, Arizona (Mr Muranko).

Address correspondence to: Philip Harber, MD, MPH, Division of Occupational & Environmental Medicine, Department of Family Medicine, University of California, Los Angeles, 10940 Wilshire Blvd, Ste #1220, Los Angeles, CA 90024; E-mail: pHarber@mednet.ucla.edu.

DOI: 10.1097/01.jom.0000052955.59271.66

Carbon black is an amorphous carbon product composed of particles and fused particle aggregates produced by the controlled combustion of gaseous or liquid hydrocarbons.[1] The material is used primarily as a filler in automotive rubber products such as tires, constituting approximately one-third of a tires weight. It is also used as a pigment in printing inks, paints and toners.

The chemical structure is extremely simple, consisting nearly completely of pure inorganic carbon. The physical characteristics of the particles differ depending upon the application for which it is intended. In the production reactor primary particles aggregate and agglomerate into larger particles, and most carbon blacks are pelletized to facilitate handling. Airborne carbon black particulate is typically in a size range small enough to be inhaled, but most particles exceed the ultrafine particle size range (Kuhlbusch, unpublished results). Because the particle size permits inhalation, there has been concern about respiratory effects.

Although several studies suggested that there was no significant effect of inhalation[2–5] others have shown relationships between long-term cumulative exposure and spirometric, radiographic, and symptomatic effects of limited magnitude.[5–7] Gardiner et al.[5] felt that there were methodologic limitations of many of the early studies.

Extensive changes in production processes and control measures have been instituted over the past several decades, resulting in substantial declines in exposure.[1,8] The North

TABLE 1
Characteristics OF Participants

A. By Plant and Overall

			Tenure in Industry			Age	
Plant	Number	% Female	Mean	(SD)	Range	Mean	(SD)
All	1755	9%	14.1	9.7	0.0–53.7	43.7	9.1
1	136	15%	15.9	8.4	0.2–37.8	44.7	8.2
2	115	7%	16.6	8.6	0.6–40.3	46.3	8.0
3	62	15%	17.4	10.2	0.0–48.0	42.7	7.4
4	99	9%	14.9	9.6	0.2–33.3	42.6	9.5
5	43	9%	11.6	10.3	0.1–32.8	42.6	8.4
6	196	7%	14.7	10.4	0.0–38.6	45.0	9.6
7	58	12%	13.2	9.1	0.4–33.8	43.4	9.5
8	24	8%	18.3	9.9	0.7–37.5	45.3	8.8
9	49	6%	12.8	9.4	0.4–37.5	41.0	9.6
10	119	3%	13.1	9.8	0.3–53.7	45.6	8.3
11	55	4%	9.8	9.5	0.1–34.3	40.2	9.4
12	84	5%	14.5	9.2	0.1–37.7	43.5	9.3
13	44	9%	13.3	8.3	0.8–32.7	46.3	8.5
14	85	9%	10.0	10.3	0.3–34.9	41.9	8.9
15	72	6%	19.0	12.0	0.1–38.7	47.6	9.3
16	75	11%	10.9	8.3	0.1–33.5	41.0	9.2
17	75	12%	15.4	8.8	0.4–37.4	44.3	9.1
18	61	7%	11.5	8.5	0.2–29.6	42.6	8.8
19	67	22%	12.7	8.4	0.0–26.8	40.9	7.5
20	73	3%	13.1	9.9	0.0–39.9	41.6	8.9
21	94	10%	13.5	9.4	0.1–39.4	42.8	10.5
22	69	6%	15.2	10.4	0.1–33.9	43.7	9.4

B. By Job Category and Overall

			Tenure in Industry			Age	
Job Category	Number	% Female	Mean	(SD)	Range	Mean	(SD)
Administration	325	32%	12.8	10.2	0.0–38.6	43.1	9.4
Laboratory	191	10%	17.9	9.9	0.1–53.7	44.8	9.2
Maintenance	586	2%	15.5	9.5	0.0–48.0	44.6	8.9
Other	21	0%	13.5	11.7	0.0–36.2	44.7	10.6
Production	384	0.3%	13.8	9.0	0.1–40.3	43.2	8.4
Warehousing	187	7%	9.1	8.1	0.0–29.8	40.9	9.7

SD = standard deviation

Participation rates are shown by plant location. Rates were calculated separately based upon those having questionnaires (Qaire) and spirometry (Spiro). The number of potential participants (eligible) was provided from plant census data. However, some workers were not present on the days of actual testing.

American carbon black industry has been conducting industry-wide medical surveillance testing for over 20 years. Results from the latest round of testing, largely conducted in 2000, were available for analysis. The current study was conducted to ascertain whether there are indeed respiratory effects, and if so, to quantify the dose-effect relationships.

Methods

Participants

Twenty-two plants participated. Two plants were in Canada, and the remainder were in the United States. Data were collected as part of routine medical surveillance testing, and each company informed workers of their clinical results. For research purposes, a data set without personal identifier links to individuals was created.

A standardized system for job titles was developed. Major job categories are summarized in Table 1. Job titles are organized into a series of five major and one miscellaneous job categories: administration, laboratory, maintenance, production, warehouse/materials handling, and other.

Each of these categories includes more specific job titles. A preliminary survey led to selection of this scheme to optimize separation according to tasks, applicability across plants, applicability over time (ie, applicable to work histories in the past), and consistency with other studies.

The number of participants for each of the plants are summarized in Table 1. Based upon company census data, the overall participation rate was 87% for questionnaires and 83%

for spirometry. Participation rates for individual plants varied from 64% through 100%; only one plant had a participation rate below 70%.

Data were collected as part of routine periodic workplace and worker surveillance activity of the North American carbon black industry. The participation of individual workers in the medical surveillance activity is voluntary. Each company chose the tests to perform, but as a minimum, they included a standardized questionnaire, spirometry, PA chest radiograph, and work history.

Characteristics of the participants are summarized in Tables 1a and 1b. Most were male (91%); 11% were nonwhite (African-American). All participants spoke English.

Most of the participating employees had worked in industry for many years; the average tenure in the carbon black industry was 14.1 years.

Smoking status was based upon self-reports in the questionnaires. Percentages are derived from those who answered all tobacco related questions. Overall, 53% reported being nonsmokers, 22% were current smokers, and 25% reported that they were ex-smokers. Among the plants, the percentage of nonsmokers varied from 42 to 69%.

Spirometry

Spirometry was performed by a contractor, Continuum Inc. (San Diego, CA) using a pneumotachograph spirometer (Koco, Denver CO). Technicians performing the spirometry are certified for completion of the NIOSH cotton dust spirometry course. Spirometers were calibrated at least daily, and there was an active quality assurance program. Test performance methodology followed the recommendations of the American Thoracic Society (ATS).[9] Spirometry in Canada was performed by contracted clinics according to ATS criteria.

Questionnaire

A standardized questionnaire was developed and pilot tested for the medical surveillance activity. It included questions about job history in the carbon black industry, other job history, respiratory symptoms, respiratory history, allergy symptoms, and tobacco use. Many of the respiratory symptoms questions were directly derived from the American Thoracic Society questionnaire.[10] The questionnaire was provided to participants several days before testing. Each was asked to complete it before coming to the testing location. A trained interviewer was present to check for completeness of the questionnaires. Interviewers were explicitly trained to avoid making any biasing statements to study participants.

Communication of Clinical Test Results

Data from the spirometry, chest radiography, and any optional testing selected by individual companies were clinically interpreted and reported to the individual worker according to each company's medical department's routine method. In addition, for medical surveillance program quality assurance purposes, a proportion of the spirograms and radiographs were reviewed by an external consultant for technical adequacy. Several unannounced site visits were conducted during testing.

Worker Job Histories

A systematic approach to obtaining job histories was used. Reliance upon personnel records was avoided because record systems differed greatly from plant to plant. In addition, there was considerable variability among plants in job titles used. For these reasons, a consensus set of job titles was selected, and those completing questionnaires were asked to use the most relevant job title, even if that title did not actually exist in the plant. Furthermore, individuals could designate several different job titles for the same period of time. The set of job titles to be used was based upon consensus and a small pilot trial. In addition, as part of the Process Survey described below, plant safety and management personnel were asked about which job titles were relevant to their plant and whether the proposed set excluded any major worker groups in their facility.

If the subject described conducting multiple jobs over the same time (eg, because a single narrow job title did not adequately describe the work), the number of months allocated to each was proportionally decreased eg, a worker spending a full year splitting time between the jobs of maintenance-utility and maintenance-other was assigned the equivalent of six months to each.

Determining Recent and Cumulative Worker Exposures

The methodology used for creating the job exposure matrix and for determining recent and cumulative exposures for each participant are described in more detail elsewhere.[11] Cumulative and recent exposures to carbon black were calculated for each participant. A three-step process was used for estimating exposures for each person:

1. An "historic" job-exposure matrix was developed to summarize typical exposures by job title or job category for each plant for each year.
2. The job title and plant for each year of employment in the industry were determined for each individual from the employment history,.
3. The data in the historic job exposure matrix were then used to calculate exposures to carbon black for each participant. For each year of carbon black industry employment, the appropriate historic job exposure matrix exposure cell was identified for the job category/plant/year tuple, and the total exposure over the working lifetime for the individual was determined as the sum. For the "recent exposures," a combination of job title and plant was used to describe exposure based upon the year 2000 industrial hygiene survey (Muranko, unpublished results).

Characterizing "Historical" Exposures According to Plant and Job

Three methods were integrated for creating the job exposure matrix. Results of each of the methods were then integrated to produce quantitative measures of cumulative exposure for individual workers. These three methods were as follows: 1) industrial hygiene air level measurement (both recent and those from the past); 2) systematic survey of processes used; and 3) a semi-quantitative historical exposure rating scale instrument. These were complemented by discussion with experts and plant visits.

Statistical Methods

The spirometry and questionnaire data were coded to remove personal identifiers. The resulting data set was provided to the research team for analysis. Although individual subjects could not be identified, the plant of employment was identified. Data were managed using a commercial relational database (Microsoft Access), and statistical calculations were done using SAS for personal computers (SAS Institute, Cary, NC). Where appropriate, descriptive statistics, multiple linear regression, multiple logistic regression, and frequency table analyses were utilized.

Spirometry data were available for 1560 subjects. Data were analyzed by multiple linear regression using several models. In all, results were stratified by gender. Spirometry values of nonwhite subjects were multiplied by 1.12 to facilitate comparability. Because of the relatively few females in the data set, their results are not reported here.

For analysis of possible relationships between exposure and symptoms, subjects were divided into five groups (pentiles) separately according to cumulative and recent dust exposure. Chronic bronchitis was defined using the "epidemiologic definition"[10] of cough and sputum for most days of the week for three months for two years; this required combining responses to several questions. Other symptoms analyzed included chronic sputum production and dyspnea. The frequency of the symptom in each exposure group was calculated, and statistical significance was ascertained by chi-square analysis with test for trend since the exposure categories are meaningfully ordered. Analyses were stratified by smoking status because of the well-established prominent effect of cigarette smoking per se.

Results

Exposure Profiling Results

As in other industries used with dust exposure, several different industrial hygiene measurement methods have been used in the carbon black industry. Three sampling methods measured different particle size distributions: respirable, total, and inhalable dust. Exposure estimates (cumulative and recent for respirable, inhalable, and total dust) were obtained by integrating each subject's work history with the job-exposure matrix characterizing exposures according to year, plant, and job category. There were over 15,000 job category-plant-year-exposure metrics combinations (22 plants $\times$ 6 job categories $\times$ 40 years x $\times$ metrics). The worker exposure profiles are summarized in Table 2. Results are shown overall and according to current job category. Mean cumulative exposures by job category ranged from 22 to 62 mg-years/m^3 for inhalable dust. Air levels in the past and in the current study were higher in the warehousing than production areas[8,12]. However, the mean cumulative exposures for subjects currently in each job category were comparable for these groups because of the longer duration of employment in the Production category (see Table 1).

Relationship of Spirometry Results to Exposure

Spirometry data were available for 1560 subjects. Table 3 summarizes the average values expressed as percentage of predicted, employing the norms used by each testing facility. Overall, the group has normal lung function.

Tables 4 and 5 summarize the results of the analyses relating pulmonary function to the 3 metrics of cumulative exposure. Table 4 includes results based upon cumulative exposures, whereas Table 5 is based upon recent exposures. Several linear regression models were selected prior to actual analysis to adjust results for smoking, gender etc. Each row in the tables represents a separate regression analysis. There was high collinearity among the three exposure metrics, and therefore they were not combined in a single model.

There was a small but statistically significant effect of cumulative exposure to carbon black upon the FEV_1. As shown for the first model, the estimated slope was -0.0007 L FEV_1/mg-year/m^3 of exposure to inhalable dust. For respirable and total dust exposure, the estimated slopes were -0.0087 and -0.0020, respectively.

Analyses stratified by smoking category (nonsmokers, ex-smokers, current smokers) are also shown. In these analyses, the general relationship is the same. However, because of smaller subject numbers in each analysis, results are not statistically significant at the alpha $= 0.05$ level (two-tailed test).

Similar analyses were conducted for the forced vital capacity (FVC) and the forced expiratory flow over the mid-portion of the expiratory maneuver ($FEF_{25-75\%}$). Although several of the individual regression analyses showed statistically significant relationships, results were less consistent than for FEV_1. For example, analyses of nonsmokers' FEV_1 results, but not for FVC, were consistent with the overall regression analyses. Furthermore,

TABLE 2
Worker Profile Exposure Estimates

Overall	Mean	(SD)	Range	*N*
Cumulative inhalable	48.4	56.3	0.2–415.8	1680
Cumulative 'total'	16.1	18.8	0.1–138.6	1680
Cumulative respirable	4.7	4.8	0.1–31.1	1680
Recent inhalable	1.4	1.4	0.1–09.2	1680
Recent 'total'	0.5	0.5	0.0–03.1	1680
Recent respirable	0.2	0.2	0.0–01.7	1680

	Cumulative Inhalable		Cumulative 'Total'		Cumulative Respirable	
Job Category	Mean	(SD)	Mean	(SD)	Mean	(SD)
Administration	22.7	34.8	7.6	11.6	2.3	3.1
Laboratory	51.5	47.7	17.2	15.9	4.9	4.1
Maintenance	57.3	58.3	19.1	19.4	5.6	5.1
Other	62.2	92.9	20.7	31.0	5.5	6.9
Production	52.8	54.2	17.6	18.1	5.0	4.8
Warehousing	51.8	73.7	17.3	24.6	4.5	5.5

	Recent Inhalable		Recent 'Total'		Recent Respirable	
Job Category	Mean	(SD)	Mean	(SD)	Mean	(SD)
Administration	0.4	0.6	0.1	0.2	0.1	0.1
Laboratory	1.0	1.0	0.3	0.3	0.2	0.1
Maintenance	1.5	1.4	0.5	0.5	0.3	0.2
Other	1.3	1.6	0.4	0.5	0.3	0.3
Production	1.3	1.3	0.4	0.4	0.3	0.2
Warehousing	3.1	1.6	1.0	0.5	0.4	0.2

Results are shown in mg-years/m^3 for cumulative and mg/m^3 for recent exposures. sd = standard deviation. FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity.

TABLE 3
FEV_1, FVC (% Predicted) By Current Job Category (2000)

	FEV_1 Percent Predicted			FVC Percent Predicted		
Job Category	*N*	Mean	sd	*N*	MEAN	sd
Administrative	236	99	14	236	104	15
Laboratory	141	99	15	141	104	14
Maintenance	412	98	15	412	103	15
Other	15	96	20	15	103	14
Production	416	98	14	416	104	13
Warehousing	339	100	15	339	106	13

The results of average percentage of predicted (based upon each testing facility's norms) are shown by job category.

where associations were noted, the regression coefficients were not as large relative to the mean magnitude of the FVC. As shown in Table 3, results for both FEV_1 and FVC for the worker population appeared normal in comparison to external reference norms (ie, as percentage of predicted); however, the percentage predicted FVCs tended to be higher than percentage predicted FEV_1.

For recent exposure, unlike the results for cumulative exposure, no significant relationships between exposure and spirometry results were seen.

Relationships Between Symptoms and Exposure

Table 6 summarizes the analyses of relationships between cumulative exposure (expressed as pentile) and symptoms. For these analyses, subjects were grouped into pentiles according to cumulative or recent exposure; analyses are stratified for smoking status and limited to males.

A statistically significant relationship between chronic bronchitis and cumulative exposure was seen only in nonsmoking males. The effect was seen only in the two pentile groups with the highest cumulative exposures. For example, 9% of nonsmoker males in the highest exposure pentile (average cumulative exposure of 138 mg years/m^3 inhalable dust) had chronic bronchitis in comparison to 5% in the group with the lowest cumulative exposures. There was no relationship of cumu-

TABLE 4
Relationships Between Cumulative Exposure and Respiratory Function

Subjects	N	Dust			Smoking Status		Age	Height
		'TOT'	INH	RSP	Current	Ex-		
FEV_1								
Males	1427	**−0.0020**			**−0.1849**	−0.0369	**−0.0333**	**0.0159**
Male current smokers	264	−0.0010					**0.0429**	**0.0935**
Male ex smokers	294	0.0007					**−0.0384**	**0.0990**
Male never smokers	616	−0.0021					**−0.0242**	**0.1060**
Males	1427		**−0.0007**		**−0.1849**	−0.0369	**−0.0333**	**0.0159**
Male current smokers	264		−0.0003				**−0.0429**	**0.0935**
Male ex smokers	294		0.0002				**−0.0384**	**0.0990**
Male never smokers	616		−0.0007				**−0.0242**	**0.1060**
Males	1427			−0.0087	**−0.1839**	−0.0359	**−0.0330**	**0.0159**
Male current smokers	264			−0.0078			**−0.0419**	**0.0931**
Male ex smokers	294			0.0010			**−0.0380**	**0.0990**
Male never smokers	616			−0.0060			**−0.0246**	**0.1060**
FVC								
Males	1427	**−0.0024**			−0.0945	0.0011	**−0.0348**	**0.0239**
Male current smokers	264	−0.0009					**−0.0419**	**0.1386**
Male ex smokers	293	0.0009					**−0.0417**	**0.1616**
Male never smokers	609	−0.0012					**−0.0273**	**0.1571**
Males	1427		**−0.0008**		−0.0945	0.0011	**−0.0348**	**0.0239**
Male current smokers	264		−0.0003				**−0.0419**	**0.1386**
Male ex smokers	293		0.0003				**−0.0417**	**0.1616**
Male never smokers	609		−0.0004				**−0.0273**	**0.1571**
Males	1427			**−0.0111**	**−0.0931**	0.0023	**−0.0342**	**0.0239**
Male current smokers	264			−0.0094			**−0.0404**	**0.1381**
Male ex smokers	293			0.0023			**−0.0414**	**0.1617**
Male never smokers	609			−0.0034			**−0.0275**	**0.1572**
FEF								
Males	1427	−0.0025			**−0.4633**	−0.1016	**−0.0395**	0.0059
Male current smokers	264	−0.0015					**−0.0590**	**0.0515**
Male ex smokers	293	0.0018					**−0.0430**	**0.0201**
Male never smokers	609	−0.0041					**−0.0258**	**0.0485**
Males	1427		−0.0008		**−0.4633**	−0.1016	**−0.0395**	0.0059
Male current smokers	264		−0.0005				**−0.0590**	**0.0515**
Male ex smokers	293		0.0006				**−0.0430**	0.0201
Male never smokers	609		−0.0014				**−0.0258**	**0.0485**
Males	1427			−0.0090	**−0.4630**	−0.1003	**−0.0395**	0.0059
Male current smokers	264			−0.0078			**−0.0585**	**0.0513**
Male ex smokers	293			0.0043			**−0.0425**	0.0202
Male never smokers	609			−0.0109			**−0.0267**	**0.0486**

Results are shown in units of liters for FEV_1 & FVC, liters/min for $FEF_{25-75\%}$ (FEF), cm for height, and mg- yrs/m^3 for cumulative and mg/m3 for recent exposures. Models including smoking status as a variable compare current and ex-smokers to never smokers. Results with $P <=$ 0.05 are shown in bold. 'TOT' = total; INH = inhale; RSP = respirable dust.

lative exposure with either dyspnea or chronic sputum production. Although not statistically significant, a similar trend was noted for chronic sputum production. No trend was seen for dyspnea.

The effect of smoking was much greater than the effect of carbon black exposure. Among current smokers, chronic bronchitis was much more common than among the never smokers. Among current smokers, no relationship was seen between cumulative exposure and chronic bronchitis or other symptoms.

As shown in table 7, there were no relationships between recent exposure (as pentile of recent exposure) and symptom frequency. Recent exposure levels are low in comparison to those of the past.

Table 8 summarizes the exposure levels associated with each of the cumulative and recent exposure pentile groups. For cumulative exposure, the highest two pentiles had considerably more exposure than the lower groups. (ie, although the number of subjects in each pentile was approximately the same, the exposures were disproportionately high in the upper two pentile groups).

Discussion

Carbon Black is widely used as a filler and pigment. The end product consists nearly completely of elemental carbon.[1,13]

TABLE 5
Relationships Between Recent Exposure and Respiratory Function

		Dust			Smoking Status			
Subjects	***N***	**'TOT'**	**INH**	**RSP**	**Current**	**Ex-**	**Age**	**Height**
FEV_1								
Males	1417	0.0379			−0.1895	−0.0335	**−0.0353**	**0.0161**
Male current smokers	264	0.1195					**−0.0432**	**0.0958**
Male ex smokers	293	0.0898					**−0.0374**	**0.0989**
Male never smokers	609	0.0365					**−0.0255**	**1.0742**
Males	1417		0.0126		**−0.1895**	−0.0335	**−0.0353**	**0.0161**
Male current smokers	264		0.0398				**−0.0432**	**0.0958**
Male ex smokers	293		0.0299				**−0.0374**	**0.0989**
Male never smokers	609		0.0122				**−0.0255**	**0.1074**
Males	1417			0.1107	**−0.1915**	−0.0358	**−0.0352**	**0.0162**
Male current smokers	264			0.1165			**−0.0435**	**0.0945**
Male ex smokers	293			0.1961			**−0.0375**	**0.0991**
Male never smokers	609			0.1321			**−0.0254**	**0.1074**
FVC								
Males	1417	0.0412			−0.0985	0.0078	**−0.0373**	**0.0240**
Male current smokers	264	0.1248					**−0.0421**	**0.1410**
Male ex smokers	293	0.0738					**−0.0405**	**0.1616**
Male never smokers	609	0.0580					**−0.0280**	**0.1575**
Males			0.0137		−0.0985	0.0078	**−0.0373**	**0.0240**
Male current smokers	264		0.0416				**−0.0421**	**0.1410**
Male ex smokers	293		0.0246				**−0.0405**	**0.1616**
Male never smokers	609		0.0193				**−0.0280**	**0.1575**
Males	1417			0.0284	−0.0964	0.0062	**−0.0374**	**0.0239**
Male current smokers	264			−0.0120			**−0.0426**	**0.1388**
Male ex smokers	293			0.1008			**−0.0407**	**0.1618**
Male never smokers	609			0.0940			**−0.0282**	**0.1572**
FEF								
Males	1417	0.0502			−0.4694	−0.0977	**−0.0417**	0.0063
Male current smokers	264	0.0920					**−0.0599**	**0.0535**
Male ex smokers	293	0.1370					**−0.0408**	0.0200
Male never smokers	609	0.0490					**−0.0284**	**0.0509**
Males	1417		0.0167		−0.4694	−0.0977	**−0.0417**	0.0063
Male current smokers	264		0.0307				**−0.0599**	**0.0535**
Male ex smokers	293		0.0457				**−0.0408**	0.0200
Male never smokers	609		0.0163				**−0.0284**	**0.0509**
Males	1417			0.2728	−0.4781	−0.1022	**−0.0414**	0.0065
Male current smokers	264			0.2458			**−0.0597**	**0.0533**
Male ex smokers	293			0.3654			**−0.0409**	0.0204
Male never smokers	609			0.2752			**−0.0280**	**0.0512**

See prior table for definitions of symbols.

Early studies of respiratory effects were inconsistent. Some suggested the absence of a significant respiratory health effect,[2–4] whereas other studies suggested more serious adverse effects. Many of the studies were reviewed and considered to be methodologically flawed by Gardiner et al.[5] A large multi-phase study of Western European carbon black production plants was conducted between 1987 and 1995 by Gardiner et al.[14,15] The study included questionnaires, spirometry conducted by plant personnel, chest radiography, and measurement of air levels of carbon black. The authors concluded that carbon black is associated with reduction in lung function, chest radiographic findings, and excess symptoms of chronic bronchitis and sputum production. In particular, associations were noted between cumulative exposure and FEV_1, but not between exposure and FVC. An increased prevalence of low profusion radiographic abnormalities was also associated with higher cumulative exposures.[6]

The study reported herein was conducted for several reasons. It sought to determine if the relationships reported in the European study are present in North American production facilities. Unlike Europe, where several different production processes have been used, (Harber, unpublished results), nearly all in North America have used the oil furnace method since at least the late 1950 seconds.

The current study sought to develop a more precise estimate of the dose-response relationship between exposure and health effect to provide an appropriate guide for regulatory

TABLE 6
Relationship Between Symptoms and Cumulative Carbon Black Exposure

CHRONIC BRONCHITIS

Group	'Total' Dust Pentile				
	1	2	3	4	5
Male never smoker	5%	6%	4%	9%	9%
Male ex-smoker	5%	8%	9%	8%	4%
Male current smoker	27%	25%	32%	32%	28%

Group	Inhalable Dust Pentile				
	1	2	3	4	5
Male never smoker	5%	6%	4%	10%	9%
Male ex-smoker	5%	8%	9%	8%	4%
Male current smoker	27%	25%	32%	32%	28%

Group	Respirable Dust Pentile				
	1	2	3	4	5
Male never smoker	5%	6%	7%	7%	10%
Male ex-smoker	5%	9%	8%	8%	4%
Male current smoker	30%	26%	29%	39%	23%

CHRONIC SPUTUM

Group	'Total' Dust Pentile				
	1	2	3	4	5
Male never smoker	3%	3%	6%	5%	5%
Male ex-smoker	0%	5%	7%	8%	1%
Male current smoker	16%	21%	27%	14%	24%

Group	Inhalable Dust Pentile				
	1	2	3	4	5
Male never smoker	3%	3%	6%	5%	5%
Male ex-smoker	0%	5%	7%	8%	1%
Male current smoker	16%	21%	27%	14%	24%

Group	Respirable Dust Pentile				
	1	2	3	4	5
Male never smoker	4%	3%	4%	6%	6%
Male ex-smoker	0%	8%	3%	9%	1%
Male current smoker	21%	18%	21%	22%	20%

DYSPNEA

Group	'Total' Dust Pentile				
	1	2	3	4	5
Male never smoker	6%	4%	13%	12%	16%
Male ex-smoker	12%	13%	19%	20%	15%
Male current smoker	12%	19%	21%	29%	20%

Group	Inhalable Dust Pentile				
	1	2	3	4	5
Male never smoker	6%	4%	13%	12%	16%
Male ex-smoker	12%	13%	19%	20%	15%
Male current smoker	12%	19%	21%	29%	20%

Group	Respirable Dust Pentile				
	1	2	3	4	5
Male never smoker	7%	4%	12%	12%	16%
Male ex-smoker	13%	14%	14%	19%	18%
Male current smoker	14%	18%	21%	28%	21%

TABLE 7
Relationship Between Symptoms and Recent Carbon Black Exposure

CHRONIC BRONCHITIS

Group	'Total' Dust Pentile				
	1	2	3	4	5
Male never smoker	7%	6%	7%	8%	4%
Male ex-smoker	4%	6%	13%	6%	4%
Male current smoker	33%	31%	26%	27%	29%

Group	Inhalable Dust Pentile				
	1	2	3	4	5
Male never smoker	7%	6%	7%	8%	4%
Male ex-smoker	4%	6%	13%	6%	4%
Male current smoker	33%	31%	26%	27%	29%

Group	Respirable Dust Pentile				
	1	2	3	4	5
Male never smoker	7%	7%	6%	7%	5%
Male ex-smoker	5%	9%	10%	5%	5%
Male current smoker	33%	29%	26%	28%	30%

CHRONIC SPUTUM

Group	'Total' Dust Pentile				
	1	2	3	4	5
Male never smoker	4%	6%	2%	3%	6%
Male ex-smoker	3%	5%	3%	7%	5%
Male current smoker	26%	28%	22%	12%	20%

Group	Inhalable Dust Pentile				
	1	2	3	4	5
Male never smoker	4%	6%	2%	3%	6%
Male ex-smoker	3%	5%	3%	7%	5%
Male current smoker	26%	28%	22%	12%	20%

Group	Respirable Dust Pentile				
	1	2	3	4	5
Male Never Smoker	4%	4%	4%	3%	6%
Male Ex-Smoker	2%	5%	5%	3%	6%
Male Current Smoker	26%	19%	25%	12%	21%

DYSPNEA

Group	'Total' Dust Pentile				
	1	2	3	4	5
Male never smoker	11%	14%	6%	13%	6%
Male ex-smoker	20%	17%	16%	14%	14%
Male current Smoker	21%	20%	20%	25%	18%

Group	Inhalable Dust Pentile				
	1	2	3	4	5
Male never smoker	11%	14%	6%	13%	6%
Male ex-smoker	20%	17%	16%	14%	14%
Male current Smoker	21%	20%	20%	25%	18%

Group	Respirable Dust Pentile				
	1	2	3	4	5
Male Never Smoker	10%	11%	12%	9%	8%
Male Ex-Smoker	17%	18%	18%	17%	12%
Male Current Smoker	24%	20%	19%	22%	20%

For each symptom and worker group, the percentage having the symptom within the pentile is shown. Exposure pentile assignments are based upon the estimated exposure to inhalable dust.

TABLE 8
Average Exposure of Each Pentile Group

	Cumulative			Recent		
Pentile	Inhalable	'Total'	Respirable	Inhalable	'Total'	Respirable
1	2.90	0.97	0.48	0.19	0.06	0.06
2	12.79	4.25	1.52	0.42	0.14	0.10
3	30.31	10.09	3.11	0.84	0.28	0.17
4	57.03	18.97	5.53	1.63	0.54	0.28
5	137.92	45.92	12.50	3.82	1.27	0.60

For each pentile, the average exposure for individuals within the pentile is noted. For cumulative exposure, units are mg-years/m^3, and for recent exposures, units are mg/m^3. Results are shown separately for inhalable, 'total', and respirable dust.

standard establishment. In particular, the current study was designed to overcome limitations in retrospective prior exposure assessments.[11]

The European study calculations were was based upon the assumption that air levels measured in the late-1980s were accurate reflections of the preceding era. However, the study found large decreases between the first and second phases, suggesting that the assumption would lead to underestimation of cumulative exposures.[6]

Industrial hygiene measurements of carbon black particulate levels have used a variety of size-selective personal sampling devices (ie, respirable, inhalable, and 'total' dust fractions). The current study therefore employs a method to interrelate the results obtained by different methods.

Finally, this study used a standardized method of questionnaire administration in order to collect information more precisely than feasible in the earlier European study, which was a multinational, multilingual study with much variability from plant-to-plant.[14]

The results confirm the presence of a statistical association between small reductions in one pulmonary function parameter and exposures associated with carbon black production. As shown in Table 4, cumulative exposure was negatively associated with FEV_1. Based upon the overall regression analyses, cumulative exposure of 1 mg-year of 'total' dust per cubic meter is associated with a reduction of FEV_1 by 2 mL. This corresponds to an estimated effect of 0.7 mL FEV_1 per mg-year/m^3 of the inhalable dust fraction. Extrapolating this to the "worst case" situation, in which an employee spends 40 years working with 1 mg/m^3 of 'total' dust exposure (equivalent to approximately 3 mg/m^3 of inhalable dust), a reduction of 80 mL FEV_1 would be associated. Similarly, a reduction of 240 mL would be estimated for an individual spending 40 years in a work environment with air levels of 3 mg 'total' dust per cubic meter (corresponding to approximately 9 mg of inhalable dust per cubic meter of air).

Although the FEV_1 was associated with *cumulative* exposures, the current study showed that there was not a statistical association with recent exposures at levels currently present in production facilities. The exposure measurement for these analyses is termed "recent" rather than "current" because actual exposure was not determined immediately before performing spirometry. Similar measurement conditions existed in the European study.

The finding of no overall relationship with recent exposures appears more likely to indicate a bona fide lack of significant effect rather than limitation of the study itself. Statistical power was enhanced by incorporating a large number of subjects. The precision of exposure estimates for recent exposures is greater than that for cumulative exposures, which relied upon reconstruction from historical data; yet, it was possible to demonstrate associations with cumulative exposure.

Although no relationship between typical recent exposures and FEV_1 reduction was noted in the overall analysis, it is theoretically possible that some individuals may have transient effects. Although the study of Kuepper et al[16] shows that carbon black does not induce airway hyper-responsiveness, very high exposures to carbon black, as for other poorly soluble dusts, may produce transient reductions in lung function, particularly in persons with pre-existing airway hyper-responsiveness. Hence, as a precautionary measure, the use of respiratory protection is advisable for situations with particularly high transient dust exposures, such as entering a baghouse.

Gardiner et al provided the first systematic study demonstrating the presence of a relationship of cumulative exposure with lung function.[15] They noted, however, that their study is likely to have underestimated cumulative exposure because 1987 conditions were assumed to be the level at which earlier exposures existed. Their qualitative assessment suggested that air levels in the European production facilities even a few years previously may have been more than double the value they used for estimating exposure retrospectively,[14] and quantitative studies because their study began confirmed continuing declines of exposure levels.[17,18] Therefore, in order to more accurately quantify the relationship of the exposures to FEV_1, the current study incorporated an historical reconstruction of exposures based upon all available prior exposure data, including a systematic North American exposure assessment completed in the late-1970s,[12] a process history questionnaire, interviews of plant personnel, and a systematic rating questionnaire completed by plant personnel.[11] In addition, development of exposure profiles for individual workers was aided by the methodologic studies of Van Tongeren[19,20] that showed for the European data set that the slope of FEV_1 to exposure relationship is maximized by combining data from narrow and broad exposure categories.

Cumulative exposures estimated in the current study showed an average of 16 mg 'total' dust-years per cubic meter. This corresponds to 48 mg inhalable dust-years per cubic meter. In contrast, Gardiner et al. estimated average cumulative exposures of 22 and 20.5 mg inhalable dust-years per cubic meter in the second and third phases of their studies (derived from their published values of 263 and 246 mg-months/m^3).[6] As noted above, this is likely to be an underestimate of the actual cumulative exposure, particularly in view of the long tenure of workers in that study (average length of employment before the initial European study was 14 years).[15]

Adjusted for the more precise and accurate exposure estimates of the current study, the magnitude of the effect of cumulative exposure upon FEV_1 appears generally comparable between the current North American and the earlier European studies. For example, Gardener et al.[6] reported a regression coefficient of -0.01 l FEV_1 per 100 mg-months/m^3 cumulative inhalable dust exposure in their phase 2/3 study. Converted to the units used in this article, this is arithmetically equivalent to -1.2 mL per mg inhalable dust-year/m^3. The current North American study found a coefficient of -0.7 mL per mg inhalable dust-year/m^3. In view of the likely underestimation of cumulative dose in the European study, the reported regression coefficients of the two studies are comparable.

This study also demonstrated that symptoms of chronic bronchitis were more frequent in those with very heavy cumulative exposures. This effect was seen only in the nonsmokers. The magnitude of the increment was limited (4%, comparing those with the very highest and lowest cumulative exposures). The effect of carbon black exposure was very small in comparison to the effect of cigarette smoking. For example, among smokers, 27% had chronic bronchitis even in the lowest exposure group, whereas among the nonsmokers, only 9% with the highest exposures report symptoms of chronic bronchitis. The data of Table 6 suggest that lower exposures did not increase the likelihood of chronic bronchitis. In addition, recent exposures, which are significantly lower than those of the past, did not appear to be associated with an increased frequency of bronchitis. It is theoretically possible that a very small effect upon increasing the frequency of chronic bronchitis occurs in smokers, but that the effect is so small in comparison to the effect of smoking itself that it is not detectable by these methods.

The strongest associations were those of long-term heavy exposure with FEV_1. This study and the European studies[6,15] both demonstrate that carbon black exposure is not associated with significant consistent reductions in the forced vital capacity. Other studies have suggested that long-term exposure is associated with an increased prevalence of minor radiographic abnormalities. The radiographic abnormalities were limited in extent; for example, in a large study, only 0.6% had radiographic findings showing profusion scores $>=$ 2/1 according to the International Labour Organization scale (Saez-Loret, unpublished data). Longitudinal follow-up from 1987–1995 of the multi-plant European cohort[7] and long-term follow-up of persons with minor abnormalities over 25 years in one plant (Harber, unpublished results) do not show progression to advanced pneumoconiosis. The paucity of high profusion radiographic findings, the absence of progression to extensive radiographic abnormality, and the absence of restrictive physiologic abnormalities suggest that carbon black does not lead to a fibrotic pneumoconiosis. The data suggest that the limited effect found is upon the airways per se.

In the recent North American and Western European carbon black studies, exposures have been measured by three different methods. The North American studies have used a traditional method thought to measure 'total' particulate (37-mm closed-face filter cassette), as well as a method to measure the respirable fraction (particles less than 10 μm, aerodynamic diameter). The Western European studies have measured respirable and inhalable (particles less than 100 μm, aerodynamic diameter) aerosol fractions. Subsequent comparative sampler head studies in U.S. carbon black manufacturing environments have determined that the traditional total dust method underestimates the actual inhalable fraction of carbon black dust by nearly a factor of three.[21] At the current time, inhalable dust measurements appear to be the most preferable metric for assessing exposure. Respirable dust levels are typically quite low, increasing the likelihood of obtaining many nondetectable samples. The biologic considerations suggested by this study support the use of an inhalable fraction dust standard. Particle sampling for respirable size dust is particularly relevant for diseases characterized by alveolitis and interstitial fibrosis.[22] Measurement of particles in the inhalable dust size range is therefore most relevant for airway effect as reflected in the FEV_1.

In summary, this study confirms the presence of a relationship between cumulative exposure to high levels of carbon black in production facilities and small reductions in FEV_1 and a slightly increased prevalence of chronic bronchitis. These data extend the European studies by providing a quantitative estimate of the dose-response relationship considering historic exposures, which have declined remarkably over the past several decades. Information on the dose-effect relationships from this study may contribute to voluntary and regulatory standard-setting. Further research is necessary to determine if carbon black per se or other contaminants present in the production facilities but not in the end product are responsible for the effect demonstrated. Furthermore, because the magnitude of the effect is small, the current study does not permit distinguishing whether it is due to unique characteristics of this material or reflects effects that would be seen with any poorly soluble inorganic dust.

Acknowledgment

The authors thank the plant safety coordinators, the medical directors of the companies involved, and particularly the participating workers. In addition, the authors acknowledge the invaluable assistance of Nerisa Garcia, Cynthia Acosta, Tilly Oren, and Dr Steven Shvartsblat in this work. This work was supported by a research contract from the International Carbon Black Association.

References

1. McCunney RJ, Muranko H, Valberg P. Carbon Black. In: Bingham E, Cohrssen B, Powell CH, eds. *Patty's Industrial Hygiene and Toxicology*. Vol. 8. New York: John Wiley and Sons; 2000.
2. Crosbie WA. The respiratory health of carbon black workers. *Arch Environ Health.* 1986;41:346–353.
3. Kupper HU, Breitstadt R, Ulmer WT. Effects on the lung function of exposure to carbon black dusts. Results of a study carried out on 677 members of staff of the DEGUSSA factory in Kalscheuren/Germany. *Int Arch Occup Environ Health.* 1996;68:478–483.
4. Robertson JM, Ingalls TH. A case-control study of circulatory, malignant, and respiratory morbidity in carbon black workers in the United States. *Am Ind Hyg Assoc J.* 1989;50:510–515.
5. Gardiner K. Effects on respiratory morbidity of occupational exposure to carbon black: a review. *Arch Environ Health.* 1995;50:44–60.
6. Gardiner K, van Tongeren M, Harrington M. Respiratory health effects from exposure to carbon black: results of the phase 2 and 3 cross sectional studies in the European carbon black manufacturing industry. *Occup Environ Med.* 2001;58:496–503.
7. van Tongeren MJ, Gardiner K, Rossiter CE, Beach J, Harber P, Harrington MJ. Longitudinal analysis of chest radiographs from the European carbon black respiratory morbidity study. *Eur Respir J.* 2002;20:417–425.
8. Muranko H, Hethmon T, Smith R. "Total" and respirable dust exposures in the U. S. carbon black manufacturing industry. *Am Ind Hyg Assoc J.* 2001;62:57–64.
9. American Thoracic Society. Standardization of spirometry, 1994 update. *Am J Respir Crit Care Med.* 1994;152:1107–1136.
10. Ferris BG. Epidemiology standardization project (American Thoracic Society). *Am Rev Respir Dis.* 1978;118:1–120.
11. Harber P, Muranko H, Shvartsblat S, Solis S, Torossian A, Oren T. A Triangulation approach to historical job exposure assessment for the carbon black industry. J Occup Environ Med. 2003;45:131–143.
12. Smith R, Musch D. Occupational exposure to carbon black: a particulate sampling study. *Am Ind Hyg Assoc J* 1982;43:925–930.
13. IARC. Printing Processes and Printing Inks, Carbon Black and Some Nitro Compounds. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Vol. 65. Lyon: IARC; 1996.
14. Gardiner K. The methodological problems of multinational epidemiological studies with particular reference to carbon black studies. *Occup Med (Lond).* 1995;45:247–255.
15. Gardiner K, Trethowan NW, Harrington JM, Rossiter CE, Calvert IA. Respiratory health effects of carbon black: a survey of European carbon black workers. *Br J Ind Med.* 1993;50:1082–1096.
16. Kuepper H, Breidstadt R, Ulmer W. Pulmonary function testing among employees exposed to carbon black dust. *Appl Occup Environ Hyg.* 1996;11:954–961.
17. Gardiner K, Calvert IA, van Tongeren MJ, Harrington JM. Occupational exposure to carbon black in its manufacture: data from 1987 to 1992. *Ann Occup Hyg.* 1996;40:65–77.
18. van Tongeren MJ, Kromhout H, Gardiner K. Trends in levels of inhalable dust exposure, exceedance and overexposure in the European carbon black manufacturing industry. *Ann Occup Hyg.* 2000;44:271–280.
19. van Tongeren MJ, Kromhout H, Gardiner K, Calvert IA, Harrington JM. Assessment of the sensitivity of the relation between current exposure to carbon black and lung function parameters when using different grouping schemes. *Am J Ind Med.* 1999;36:548–556.
20. van Tongeren M, Gardiner K, Calvert I, Kromhout H, Harrington JM. Efficiency of different grouping schemes for dust exposure in the European carbon black respiratory morbidity study. *Occup Environ Med.* 1997;54:714–719.
21. Kerr S, Muranko H, Vincent J Personal Sampling for Inhalable Aerosol Exposure of Carbon Black Manufacturing Industry Workers. *Appl Occup Environ Hyg.* 2002;17:681–692.
22. Sexias N. Environmental monitoring. In: Harber MS, Balmes JR, ed. Occupational and environmental respiratory disease. St. Louis: Mosby, 1996:154–156.