EXHIBIT 1

&INDUSTRY_SECTOR=3273&FLD=RELLBY&FLD=TSFDSP&FLD=RE_TOLBY&sort_fmt=2&TopN=100&STATE=ALL+STATES&COUNTY=All+counties&CHEMICAL=N458&YEAR=2009&RCC=LOB&FONT_WIDTH=normal&FONT_STYLE=roman&FONT_WEIGHT=bold&_SERVICE=oiaa&_PROGRAM=xp_tri.sasmacr.tristart.macro

Releases: Facility Report

Detail columns are collapsed by default. Click the ◀▶ icon to view additional columns. Use your Browser back feature to collapse.

Data source: Release Year 2009 National Analysis data set released to the public in December 2010 See Note

TRI On-site and Off-site Reported Disposed of or Otherwise Released (in pounds), all 73 facilities, for facilities in Cement (3273), MERCURY COMPOUNDS, U.S., 2009

Row #	Facility	Total On-site Disposal or Other Releases	Total Off-site Disposal or Other Releases	Total On- and Off-site Disposal or Other Releases
1	ASH GROVE CEMENT CO. 33060 SHIRTTAIL CREEK RD, DURKEE, Oregon 97905 (BAKER)	1,962	.	1,962
2	LEHIGH SOUTHWEST CEMENT CO. 13573 TEHACHAPI BLVD, TEHACHAPI, California 93561 (KERN)	712	.	712
3	LEHIGH SOUTHWEST CEMENT CO. 24001 STEVENS CREEK BLVD, CUPERTINO, California 95014 (SANTA CLARA)	427	.	427
4	LAFARGE MIDWEST INC. 1435 FORD AVE, ALPENA, Michigan 49707 (ALPENA)	312	.	312
5	BUZZI UNICEM USA - GREENCASTLE PLANT. 3301 S COUNTY RD 150 W, GREENCASTLE, Indiana 46135 (PUTNAM)	280	1	282
6	LEHIGH CEMENT CO. 675 QUAKER HILL RD, UNION BRIDGE, Maryland 21791 (CARROLL)	247	.	247
7	TXI RIVERSIDE CEMENT ORO GRANDE PLANT. 19409 NATIONAL TRAILS HWY, ORO GRANDE, California 92368 (SAN BERNARDINO)	238	.	238
8	CONTINENTAL CEMENT CO LLC. 10107 HWY 79, HANNIBAL, Missouri 63401 (RALLS)	206	.	206
9	ASH GROVE CEMENT- LEAMINGTON UTAH. HWY 132 6 MILES E OF LEAMINGTON, LEAMINGTON, Utah 84638 (JUAB)	157	.	157
10	ASH GROVE CEMENT CO. 4457 HWY 108, FOREMAN, Arkansas 71836 (LITTLE RIVER)	151	3	154
11	LAFARGE BUILDING MATERIALS INC. 1916 RT 9W, RAVENA, New York 12143 (ALBANY)	145	0	145
12	ESSROC CEMENT CORP. 3938 EASTON NAZARETH HWY, NAZARETH, Pennsylvania 18064 (NORTHAMPTON)	130	.	130
13	BUZZI UNICEM USA - CAPE GIRARDEAU. 2524 S SPRIGG ST, CAPE GIRARDEAU, Missouri 63701 (CAPE GIRARDEAU)	116	.	116
14	ASH GROVE CEMENT CO. 3801 E MARGINAL WAY SO, SEATTLE, Washington 98134 (KING)	112	.	112
15	ASH GROVE CEMENT CO. 1801 N SANTA FE, CHANUTE, Kansas 66720 (NEOSHO)	107	.	107
16	LEHIGH CEMENT CO LLC. 700 25TH ST, MASON CITY, Iowa 50401 (CERRO GORDO)	99	.	99
17	KEYSTONE CEMENT CO. RT 329, BATH, Pennsylvania 18014 (NORTHAMPTON)	83	0	83
18	CALPORTLAND CO MOJAVE PLANT. 9350 OAK CREEK RD, MOJAVE, California 93502 (KERN)	81	.	81
19	CALIFORNIA PORTLAND CEMENT COCOLTON PLANT. 695 S RANCHO AVE, COLTON, California 92324 (SAN BERNARDINO)	74	.	74
20	CEMEX MIAMI. 1200 NW 137 AVE, MIAMI, Florida 33182 (MIAMI-DADE)	64	.	64
21	GIANT CEMENT CO. HWY 453 & I-26 (654 JUDGE ST), HARLEYVILLE, South Carolina 29448 (DORCHESTER)	61	0	61
22	RIVER CEMENT CO (DBA BUZZI UNICEM USA). 1000 RIVER CEMENT RD, FESTUS, Missouri 63028 (JEFFERSON)	60	.	60
23	ROANOKE CEMENT CO LLC. 6071 CATAWBA RD, TROUTVILLE, Virginia 24175 (BOTETOURT)	56	.	56
24	TXI OPERATIONS LP - HUNTER CEMENT PLANT. 7781 FM 1102, NEW BRAUNFELS, Texas 78132 (COMAL)	51	.	51
25	ASH GROVE TEXAS LP. 900 GIFCO RD, MIDLOTHIAN, Texas 76065 (ELLIS)	49	.	49
26	FLORIDA ROCK INDUSTRIES INC-THOMPSON S BAKER CEMENT PLANT. 4000 NW COUNTY RD 235, NEWBERRY, Florida 32669 (ALACHUA)	48	.	48
27	ESSROC CEMENT CORP. HWY 31, SPEED, Indiana 47172 (CLARK)	46	.	46
28	LEHIGH CEMENT CO LLC. 8401 SECOND AVE, LEEDS, Alabama 35094 (JEFFERSON)	45	.	45
29	TEXAS LEHIGH CEMENT CO LP. 701 CEMENT PLANT RD, BUDA, Texas 78610 (HAYS)	44	.	44
30	LAFARGE BUILDING MATERIALS INC. 463 JUDGE ST, HARLEYVILLE, South Carolina 29448 (DORCHESTER)	41	.	41
31	LAFARGE MIDWEST INC JOPPA PLANT. 2500 PORTLAND RD, GRAND	39	.	39

	CHAIN, Illinois 62953 (MASSAC)			
32	SUWANNEE AMERICAN CEMENT. 5117 US HWY 27, BRANFORD, Florida 32008 (LAFAYETTE)	38	.	38
33	HOLCIM (US) INC - CLARKSVILLE PLANT. 14738 HWY 79, CLARKSVILLE, Missouri 63336 (PIKE)	37	.	37
34	ESSROC CEMENT CORP. STATE RD 25 SOUTH 3084 W CR. 225 S, LOGANSPORT, Indiana 46947 (CASS)	37	.	37
35	LAFARGE BUILDING MATERIALS INC - ROBERTA PLANT. 8039 HWY 25 W, CALERA, Alabama 35040 (SHELBY)	35	.	35
36	MOUNTAIN CEMENT CO. 5 SAND CREEK RD, LARAMIE, Wyoming 82070 (ALBANY)	34	.	34
37	CALPORTLAND CO - RILLITO PLANT. 11115 N CASA GRANDE HWY, RILLITO, Arizona 85654 (PIMA)	33	.	33
38	LAFARGE MIDWEST INC (INCLD SYSTECH ENVIRONMENTAL). 1400 S CEMENT RD, FREDONIA, Kansas 66736 (WILSON)	30	7	37
39	LAFARGE NA. 5400 W MARGINAL WAY SW, SEATTLE, Washington 98106 (KING)	30	0	30
40	LAFARGE NA WHITEHALL PLANT. 5160 MAIN ST, WHITEHALL, Pennsylvania 18052 (LEHIGH)	28	.	28
41	LEHIGH SOUTHWEST CEMENT CO. 15390 WONDERLAND BLVD, REDDING, California 96003 (SHASTA)	28	.	28
42	HOLCIM(US). 1260 SECURITY RD, HAGERSTOWN, Maryland 21742 (WASHINGTON)	25	.	25
43	HOLCIM (US) INC HOLLY HILL PLANT. 200 SAFETY ST / HWY 453, HOLLY HILL, South Carolina 29059 (ORANGEBURG)	25	.	25
44	HOLCIM (US) INC. 6446 RT 9W, CATSKILL, New York 12414 (GREENE)	23	.	23
45	ESSROC CEMENT CORP. 17 SECOND ST, BESSEMER, Pennsylvania 16112 (LAWRENCE)	23	1	24
46	HOLCIM (US) INC DEVIL'S SLIDE PLANT. 6055 E CROYDON RD, MORGAN, Utah 84050 (MORGAN)	23	.	23
47	CEMEX KOSMOS CEMENT CO. 15301 DIXIE HWY, LOUISVILLE, Kentucky 40272 (JEFFERSON)	22	0	22
48	LAFARGE NORTH AMERICA. 2200 N COURTNEY RD, SUGAR CREEK, Missouri 64050 (JACKSON)	22	.	22
49	ASH GROVE CEMENT CO. 16215 HWY 50, LOUISVILLE, Nebraska 68037 (CASS)	22	.	22
50	LAFARGE NA (INCLUDING SYSTECH ENV CORP). 11435 COUNTY RD 176, PAULDING, Ohio 45879 (PAULDING)	21	0	21
51	SIGNAL MOUNTAIN CEMENT CO DBA BUZZI UNICEM USA. 1201 SUCK CREEK RD, CHATTANOOGA, Tennessee 37405 (HAMILTON)	20	.	20
52	LAFARGE NORTH AMERICA. 301 E FRONT ST, BUFFALO, Iowa 52728 (SCOTT)	20	.	20
53	PHOENIX CEMENT CO. 3000 W CEMENT PLANT RD, CLARKDALE, Arizona 86324 (YAVAPAI)	19	.	19
54	TXI OPERATIONS LP. 245 WARD RD, MIDLOTHIAN, Texas 76065 (ELLIS)	19	.	19
55	HOLCIM (TEXAS) LP. 1800 DOVE LN, MIDLOTHIAN, Texas 76065 (ELLIS)	18	.	18
56	DRAGON PRODUCTS CO. 107 NEW COUNTY RD, THOMASTON, Maine 04861 (KNOX)	17	.	17
57	HOLCIM (US) INC PORTLAND PLANT. 3500 STATE HWY 120, FLORENCE, Colorado 81226 (FREMONT)	15	.	15
58	ARMSTRONG CEMENT & SUPPLY CORP. 100 CLEARFIELD RD, CABOT, Pennsylvania 16023 (BUTLER)	13	.	13
59	GCC RIO GRANDE INC. 3372 LIME RD, PUEBLO, Colorado 81004 (PUEBLO)	13	.	13
60	CEMEX SOUTHEAST LLC. 2720 HWY 341 S, CLINCHFIELD, Georgia 31013 (HOUSTON)	13	.	13
61	CEMEX DE PUERTO RICO INC. STATE RD 123, KM 80, PONCE, Puerto Rico 00731 (PONCE)	13	.	13
62	HOLCIM (US) INC - TRIDENT PLANT. 4070 TRIDENT RD, THREE FORKS, Montana 59752 (GALLATIN)	10	.	10
63	CEMEX CONSTRUCTION MATERIALS SOUTH LLC. 16501 W MURPHY RD, ODESSA, Texas 79766 (ECTOR)	10	.	10
64	LEHIGH NORTHEAST CEMENT CO - GLENS FALLS PLANT. 313 WARREN ST, GLENS FALLS, New York 12801 (WARREN)	9	.	9
65	ASH GROVE CEMENT CO MONTANA CITY PLANT. 100 HWY #518, CLANCY, Montana 59634 (JEFFERSON)	8	.	8
66	ESSROC SAN JUAN INC. KM 267 STATE HWY #2, DORADO, Puerto Rico 00646 (DORADO)	7	.	7
67	CAPITOL AGGREGATES LTD CAPITOL CEMENT DIV. 11551 NACOGDOCHES RD, SAN ANTONIO, Texas 78217 (BEXAR)	5	0	5
68	CEMEX CEMENT OF TEXAS LP BALCONES PLANT. 2580 WALD RD, NEW BRAUNFELS, Texas 78132 (COMAL)	3	.	3
69	LONE STAR IND INC DBA BUZZI UNICEM USA PRYOR CEMENT PLANT. 2430 S COUNTY RD 437, PRYOR, Oklahoma 74361 (MAYES)	1	.	1
70	LAFARGE BUILDING MATERIALS INC. 2609 N 145TH E AVE, TULSA, Oklahoma 74116 (ROGERS)	1	.	1
71	LEHIGH NORTHEAST CEMENT CO - CEMENTON FACILITY. 120 ALPHA RD, CATSKILL, New York 12414 (GREENE)	0	.	0
72	LAFARGE NORTH AMERICA INC. 2150 E 130TH ST, CHICAGO, Illinois 60633 (COOK)	0	.	0
73	HOLCIM (US) INC STE GENEVIEVE PLANT. 2942 US HWY 61, BLOOMSDALE, Missouri 63627 (STE GENEVIEVE)	0	.	0

Total	7,012	12	7,024

Back to top

Export this report to a text file
Create comma-separated values, compatible with spreadsheet and databases.

Save data in comma-separated-value, CSV, file Send data into Microsoft Excel
Download all records

View other report type:
Transfers Off-site for Further Waste Management; or
Quantities of TRI Chemicals in Waste (waste management)

View report in other formats: Page Orientation:
PDF (Acrobat Reader); or Portrait; or
RTF (Microsoft Word) Landscape

Note: Reporting year (RY) 2009 is the most recent TRI data available. Facilities reporting to TRI were required to submit RY 2009 data to EPA by July 1, 2010. Facilities may submit revisions at any time. This is National Analysis dataset released to the public in December 2010 and includes updates for the years 1988 to 2009. Revisions submitted to EPA after this time are not reflected in TRI Explorer reports. TRI data may also be obtained through EPA Envirofacts.

Users of TRI information should be aware that TRI data reflect releases and other waste management activities of chemicals, not whether (or to what degree) the public has been exposedto those chemicals. Release estimates alone are not sufficient to determine exposure or to calculate potential adverse effects on human health and the environment. TRI data, in conjunction with other information, can be used as a starting point in evaluating exposures that may result from releases and other waste management activities which involve toxic chemicals. The determination of potential risk depends upon many factors, including the toxicity of the chemical, the fate of the chemical, and the amount and duration of human or other exposure to the chemical after it is released.

This report ranks the 100 largest facilities reporting in a particular disposal or other release category (by default, the report ranks the top 100 facilities by total on- and off-site disposal or other releases)). By sorting on different disposal or other release categories (e.g., Class I Wells, RCRA Subtitle C Landfills, etc.), TRI Explorer will generate a report ranking the top 100 facilities for the specific category chosen. Note that the top 100 facilities ranked for a specific category will change as the category changes (i.e., the 100 facilities ranked for Class I Wells is not necessarily the same 100 facilities for RCRA Subtitle C Landfills).

Note that if a facility name appears multiple times within the table above, the facility is a multi-establishment and submitted multiple forms for the chemical.

Off-site disposal or other releases include transfers sent to other TRI Facilities that reported the amount as on-site disposal or other release because not all states and/or not all industry sectors are included in this report.

On-site Disposal or Other Releases include Underground Injection to Class I Wells (Section 5.4.1), RCRA Subtitle C Landfills (5.5.1A), Other Landfills (5.5.1B), Fugitive or Non-point Air Emissions (5.1), Stack or Point Air Emissions (5.2), Surface Water Discharges (5.3), Underground Injection to Class II-V Wells (5.4.2), Land Treatment/Application Farming (5.5.2), RCRA Subtitle C Surface Impoundments (5.5.3A), Other Surface Impoundments (5.5.3B), and Other Land Disposal (5.5.4). Off-site Disposal or Other Releases include from Section 6.2 Class I Underground Injection Wells (M81), Class II-V Underground Injection Wells (M82, M71), RCRA Subtitle C Landfills (M65), Other Landfills (M64, M72), Storage Only (M10), Solidification/Stabilization - Metals and Metal Category Compounds only (M41 or M40), Wastewater Treatment (excluding POTWs) - Metals and Metal Category Compounds only (M62 or M61), RCRA Subtitle C Surface Impoundments (M66), Other Surface Impoundments (M67, M63), Land Treatment (M73), Other Land Disposal (M79), Other Off-site Management (M90), Transfers to Waste Broker - Disposal (M94, M91), and Unknown (M99) and, from Section 6.1 Transfers to POTWs (metals and metal category compounds only).

For purposes of analysis, data reported as Range Code A is calculated using a value of 5 pounds, Range Code B is calculated using a value of 250 pounds and Range Code C is calculated using a value of 750 pounds.

The facility may have reported multiple NAICS codes to TRI in the current reporting year. See the facility profile report by clicking on the facility name to see a list of all NAICS codes submitted to TRI for the current reporting year.

Beginning with the 2006 reporting year, the industry classification code is the North American Industry Classification System (NAICS), which has replaced the 1997 US Standard Industrial Classification (SIC) code. The primary NAICS code as reported by the facility is now used for all analysis purposes for all reporting years 2006 and later. For reporting years prior to 2006, EPA has assigned a primary NAICS code based on the SIC codes as reported for those years for the purpose of analyzing trends.

A decimal point, or "." denotes that
the facility left that particular cell blank in its Form R submission (a zero in a cell denotes either that the facility reported "0" or "NA" in its Form R submission).
"NA" in a cell denotes that the facility has submitted only Form A and thus the data for release, waste transfers or quantities of TRI chemicals in waste are not applicable. By submitting a Form A the facility has certified that its total annual reportable amount is less than 500 pounds, and that the facility does not manufacture, process, or otherwise use more than 1 million pounds of the toxic chemical.

Release:
Facility Report
Go to TRI Explorer Home | [redacted]

January 31, 2011

TOP OF SCREEN

EXHIBIT 2

&s...RELLBY&INDUSTRY=3273&FLD=RELLBY&FLD=TSFDSP&FLD=RE_TOLBY&sort_fmt=2&TopN=&STATE=06&COUNTY=All+counties&CHEMICAL=N458&YEAR=2009&BGCOLOR=...
FONT_SIZE=10+pt&FONT_WIDTH=normal&FONT_STYLE=roman&FONT_WEIGHT=bold&_SERVICE=oiaa&_PROGRAM=xp_tri.sasmacr.tristart.macro

TRI-Explorer

Last updated on Monday, January 31, 2011

Releases: Facility Report

Detail columns are collapsed by default. Click the icon to view additional columns. Use your Browser back feature to collapse.

Data source: Release Year 2009 National Analysis data set released to the public in December 2010 See Note [redacted]

TRI On-site and Off-site Reported Disposed of or Otherwise Released (in pounds), for facilities in Cement (3273), MERCURY COMPOUNDS, California, 2009

Row #	Facility	Total On-site Disposal or Other Releases	Total Off-site Disposal or Other Releases	Total On- and Off-site Disposal or Other Releases
1	LEHIGH SOUTHWEST CEMENT CO. 13573 TEHACHAPI BLVD, TEHACHAPI, California 93561 (KERN)	712	.	712
2	LEHIGH SOUTHWEST CEMENT CO. 24001 STEVENS CREEK BLVD, CUPERTINO, California 95014 (SANTA CLARA)	427	.	427
3	TXI RIVERSIDE CEMENT ORO GRANDE PLANT. 19409 NATIONAL TRAILS HWY, ORO GRANDE, California 92368 (SAN BERNARDINO)	238	.	238
4	CALPORTLAND CO MOJAVE PLANT. 9350 OAK CREEK RD, MOJAVE, California 93502 (KERN)	81	.	81
5	CALIFORNIA PORTLAND CEMENT COCOLTON PLANT. 695 S RANCHO AVE, COLTON, California 92324 (SAN BERNARDINO)	74	.	74
6	LEHIGH SOUTHWEST CEMENT CO. 15390 WONDERLAND BLVD, REDDING, California 96003 (SHASTA)	28	.	28
	Total	1,560	.	1,560

Back to top

Export this report to a text file
Create comma-separated values, compatible with spreadsheet and databases.

Save data in comma-separated-value, CSV, file   Send data into Microsoft Excel
Download all records

View other report type:
Transfers Off-site for Further Waste Management; or
Quantities of TRI Chemicals in Waste (waste management)

View report in other formats: Page Orientation:
PDF (Acrobat Reader); or   Portrait; or
RTF (Microsoft Word)   Landscape

Note: Reporting year (RY) 2009 is the most recent TRI data available. Facilities reporting to TRI were required to submit RY 2009 data to EPA by July 1, 2010. Facilities may submit revisions at any time. This is National Analysis dataset released to the public in December 2010 and includes updates for the years 1988 to 2009. Revisions submitted to EPA after this time are not reflected in TRI Explorer reports. TRI data may also be obtained through EPA Envirofacts.

Users of TRI information should be aware that TRI data reflect releases and other waste management activities of chemicals, not whether (or to what degree) the public has been exposedto those chemicals. Release estimates alone are not sufficient to determine exposure or to calculate potential adverse effects on human health and the environment. TRI data, in conjunction with other information, can be used as a starting point in evaluating exposures that may result from releases and other waste management activities which involve toxic chemicals. The determination of potential risk depends upon many factors, including the toxicity of the chemical, the fate of the chemical, and the amount and duration of human or other exposure to the chemical after it is released.

Note that if a facility name appears multiple times within the table above, the facility is a multi-establishment and submitted multiple forms for the chemical.

Off-site disposal or other releases include transfers sent to other TRI Facilities that reported the amount as on-site disposal or other release because not all states and/or not all industry sectors are included in this report.

On-site Disposal or Other Releases include Underground Injection to Class I Wells (Section 5.4.1), RCRA Subtitle C Landfills (5.5.1A), Other Landfills (5.5.1B), Fugitive or Non-point Air Emissions (5.1), Stack or Point Air Emissions (5.2), Surface Water Discharges (5.3), Underground Injection to Class II-V Wells (5.4.2), Land Treatment/Application Farming (5.5.2), RCRA Subtitle C Surface Impoundments (5.5.3A), Other Surface Impoundments (5.5.3B), and Other Land Disposal (5.5.4). Off-site Disposal or Other Releases include from Section 6.2 Class I Underground Injection Wells (M81), Class II-V Underground Injection Wells (M82, M71), RCRA Subtitle C Landfills (M65), Other Landfills (M64, M72), Storage Only (M10), Solidification/Stabilization - Metals and Metal Category Compounds only (M41 or M40), Wastewater Treatment (excluding POTWs) - Metals and Metal Category Compounds only (M62 or M61), RCRA Subtitle C Surface Impoundments (M66), Other Surface Impoundments (M67, M63), Land Treatment (M73), Other Land Disposal (M79), Other Off-site Management (M90), Transfers to Waste Broker - Disposal (M94, M91), and Unknown (M99) and, from Section 6.1 Transfers to POTWs

(metals and metal category compounds only).

For purposes of analysis, data reported as Range Code A is calculated using a value of 5 pounds, Range Code B is calculated using a value of 250 pounds and Range Code C is calculated using a value of 750 pounds.

The facility may have reported multiple NAICS codes to TRI in the current reporting year. See the facility profile report by clicking on the facility name to see a list of all NAICS codes submitted to TRI for the current reporting year.

Beginning with the 2006 reporting year, the industry classification code is the North American Industry Classification System (NAICS), which has replaced the 1997 US Standard Industrial Classification (SIC) code. The primary NAICS code as reported by the facility is now used for all analysis purposes for all reporting years 2006 and later. For reporting years prior to 2006, EPA has assigned a primary NAICS code based on the SIC codes as reported for those years for the purpose of analyzing trends.

A decimal point, or "." denotes that
the facility left that particular cell blank in its Form R submission (a zero in a cell denotes either that the facility reported "0" or "NA" in its Form R submission).
"NA" in a cell denotes that the facility has submitted only Form A and thus the data for release, waste transfers or quantities of TRI chemicals in waste are not applicable. By submitting a Form A the facility has certified that its total annual reportable amount is less than 500 pounds, and that the facility does not manufacture, process, or otherwise use more than 1 million pounds of the toxic chemical.

Release:
Facility Report
January 31, 2011

Go to TRI Explorer Home | [redacted]
TOP OF SCREEN

EXHIBIT 3

Atmospheric Environment 44 (2010) 1255–1262

Contents lists available at ScienceDirect

Atmospheric Environment

journal homepage: www.elsevier.com/locate/atmosenv

Wet deposition of mercury within the vicinity of a cement plant before and during cement plant maintenance

Sarah E. Rothenberg [a,b,*], Lester McKee [a], Alicia Gilbreath [a], Donald Yee [a], Mike Connor [a], Xuewu Fu [b,*]

[a] San Francisco Estuary Institute, 7770 Pardee Lane, Oakland, CA 94621, USA
[b] State Key Laboratory of Environmental Geochemistry, Institute of Geochemistry, Chinese Academy of Sciences, Guiyang 550002, PR China

ARTICLE INFO

Article history:
Received 19 August 2009
Received in revised form
22 December 2009
Accepted 23 December 2009

Keywords:
Mercury
Precipitation
Cement plant
Flux
Methylmercury

ABSTRACT

Hg species (total mercury, methylmercury, reactive mercury) in precipitation were investigated in the vicinity of the Lehigh Hanson Permanente Cement Plant in the San Francisco Bay Area, CA., USA. Precipitation was collected weekly between November 29, 2007 and March 20, 2008, which included the period in February and March 2008 when cement production was minimized during annual plant maintenance. When the cement plant was operational, the volume weighted mean (VWM) and wet depositional flux for total Hg (Hg_T) were 6.7 and 5.8 times higher, respectively, compared to a control site located 3.5 km east of the cement plant. In February and March, when cement plant operations were minimized, levels were approximately equal at both sites (the ratio for both parameters was 1.1). Due to the close proximity between the two sites, meteorological conditions (e.g., precipitation levels, wind direction) were similar, and therefore higher VWM Hg_T levels and Hg_T deposition likely reflected increased Hg emissions from the cement plant. Methylmercury (MeHg) and reactive Hg (Hg(II)) were also measured; compared to the control site, the VWM for MeHg was lower at the cement plant (the ratio = 0.75) and the VWM for Hg(II) was slightly higher (ratio = 1.2), which indicated the cement plant was not likely a significant source of these Hg species to the watershed.

1. Introduction

Mercury (Hg) is a global pollutant, and ingestion of fish tissue is considered the primary route for human and wildlife exposure to methylmercury (MeHg), a known neurotoxin (WHO, 1990, 1991). In the USA, more than 8500 water bodies in 45 states and territories are impaired for Hg in sediments, surface water, or fish tissue (USEPA, 2009), including many water bodies where atmospheric Hg is the primary source (e.g., MPCA, 2008; NEIWPCC, 2008). Under Section 303(d) of the Clean Water Act, impaired water bodies must be addressed through the total maximum daily load (TMDL) program, which specifies the maximum pollution load a water body can assimilate and still maintain designated beneficial uses.

It is challenging for regulators to address impairments to water bodies through the TMDL program when atmospheric sources are important (USEPA, 2008). This is partially due to inter-state boundary issues (e.g., air pollution originates out of state), and also due to regulation of air pollutants through the Clean Air Act. In California, addressing air pollutants through the TMDL program is more difficult due to a significant governmental separation between air regulation (California Air Resources Board) and water regulation (California State Water Resources Control Board). However, reducing atmospheric Hg emissions will likely result in lower fish tissue MeHg levels (Hammerschmidt and Fitzgerald, 2006; Harris et al., 2007; Hintelmann et al., 2002), as newly deposited atmospheric Hg is more rapidly converted to MeHg than native or legacy Hg (Hintelmann et al., 2002). Lowering atmospheric Hg emissions will help states meet TMDL numeric targets and restore beneficial uses, such as recreational fishing and protection of wildlife. Therefore, it is important for environmental managers to consider both atmospheric and aqueous Hg pollution inputs when developing mitigation strategies for Hg impaired water bodies.

Between 1996 and 2002, the San Francisco Bay Estuary was included on the California 303(d) List of Water-Quality Impaired Segments due to elevated Hg levels in fish tissue (USEPA, 2009). Primary Hg sources include historical gold and Hg mining, and urban and wastewater runoff (Conaway et al., 2003, 2004). In this report, Hg species (total Hg, MeHg, reactive Hg) in precipitation were characterized in the vicinity of Lehigh Hanson Permanente

* Corresponding authors at: State Key Laboratory of Environmental Geochemistry, Institute of Geochemistry, Chinese Academy of Sciences, Guiyang 550002, PR China. Tel.: +86 150 8601 2462.
E-mail addresses: rothenberg.sarah@gmail.com (S.E. Rothenberg), lester@sfei.org (L. McKee), alicia@sfei.org (A. Gilbreath), donald@sfei.org (D. Yee), mconnor@ebda.org (M. Connor), xuewu_fu@gyig.ac.cn (X. Fu).

1352-2310/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.atmosenv.2009.12.033

Cement, located in the San Francisco Bay Area (Fig. 1). Precipitation was collected weekly for 16 weeks at the cement plant from November 2007–March 2008, and within a shorter timeframe from two nearby control sites (Fig. 1). Data collection for precipitation coincided with annual cement plant maintenance in February and March 2008 (BAAQMD, 2009), which provided an ideal opportunity to compare Hg species in precipitation with and without inputs from the cement plant.

2. Site descriptions

2.1. Lehigh Hanson Permanente Cement Plant

Lehigh Hanson Permanente Cement Plant is located in the San Francisco Bay Area (hereafter referred to as "the cement plant") (latitude/longitude: 37.322432/−122.079305, elevation 183 m). Beginning in May 2007, the cement plant began reliance on petroleum coke as the sole fuel used in the kiln, and was permitted to increase usage from 7.3 to 18 metric tons (t) petroleum coke h^{-1} for fuel (Brian Bateman, BAAQMD, personal communication). From December 10–13, 2007, and a few days prior (which coincided with week 2 of precipitation collection), the cement plant was allowed to incinerate up to 19.5 t h^{-1} of petroleum coke to conduct a compliance source test.

The cement plant was chosen for this investigation as it is a significant source of Hg emissions, accounting for 29% of the 2007 total estimated Hg emissions in the San Francisco Bay Area air basin (61.4 kg/214 kg, from CARB, 2009, the most recent year data were available). The cement plant is also geographically isolated from five refineries, which account for 63% of 2007 total estimated Hg emissions in the San Francisco Bay Area air basin (134 kg/214 kg) (CARB, 2009) and are located approximately 75 km north of the cement plant. Precipitation was collected near the northern property line, downwind from the cement plant (within 0.5 km of the kiln).

2.2. Control sites and wind direction

Precipitation was collected at two nearby control sites: the rooftop of the Environmental Studies building at De Anza Community College (3.5 km east of the cement plant, latitude/longitude: 37.31622/−122.04348, elevation 91 m, "De Anza College"), and in Stevens Creek County Park (2.4 km southeast of the cement plant, latitude/longitude: 37.3056/−122.0736, elevation 152 m, "SC Park") (Fig. 1).

Wind rose plots for the sampling period were available from the La Honda climate station (~20 km east of the cement plant, elevation 229 m, data not available from the nearby Los Altos climate station) (WRCC, 2009), which indicated strongest winds originated from the west-southwest, east and east-northeast sectors.

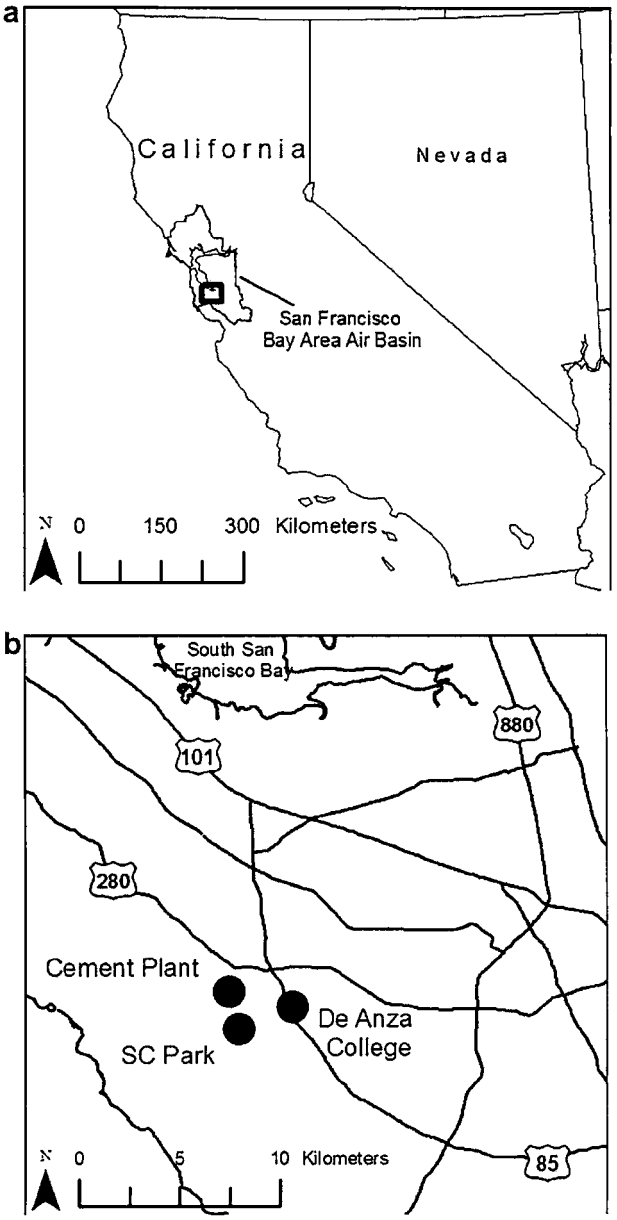


Fig. 1. Map of (a) San Francisco Bay Area Air Basin, California, USA. (b) Precipitation collection sites, including the cement plant, De Anza College and Santa Clara (SC) Park.

3. Methods

3.1. Field sampling

Precipitation was collected weekly at the cement plant and De Anza College using modified Aerochem Metrics model 301 collectors (the same used for the Mercury Deposition Network; MDN, 2009). Briefly, each collector is equipped with two covered chimneys and a moisture-sensitive plate, which activates the arm controlling the cover. The left-side chimney contained an acid-washed funnel and thistle connected to a 1-L FLPE bottle, while the right-side chimney contained an acid-washed funnel connected directly to a 1-L FLPE bottle. Side by side total Hg (Hg_T) levels indicated no significant difference in Hg_T levels between the two chimneys ($p > 0.50$, $n = 7$). At SC Park, precipitation was collected on an event basis, using an acid-washed funnel and thistle connected to a 1-L FLPE bottle, housed in a PVC tube. Collection bottles for all three sites were prefilled with either 20 ml 10% HCL (for preservation of Hg species) or 20 ml of 10% HNO_3 (to preserve other metals).

Near the cement plant precipitation was collected continuously for 16 weeks, between November 29, 2007, and March 20, 2008. At De Anza College precipitation was collected for nine weeks (January 10-March 20, 2008, weeks 8–16), and at SC Park precipitation was collected during two rain events, one occurring in February (week 13) and one in March (week 16). During the four-month period, no precipitation occurred during 5 weeks (weeks 4, 7, 11, 14, 15); additionally, during week 6 precipitation was collected for one day only near the cement plant, due to equipment damage following a powerful storm. When calculating Hg_T deposition for the 4-month period (see below and Section 4.1), only one day of precipitation was included for week 6.

Hg_T deposition (ng m^{-2} $week^{-1}$) was determined from the following equation:

$$Hg_T \text{ deposition} = [Hg_T] \times \text{precipitation} \quad (1)$$

where $[Hg_T]$ represented the concentration of Hg_T in precipitation collected in one week (ng L^{-1}), and precipitation (mm) was measured by the network of rain gages maintained by the Santa Clara Valley Water District (SCVWD) ALERT system (Station 1522, located 1.6 km and 3.5 km, respectively, from the cement plant and De Anza College, Station 1510 located 4.8 km from SC Park; SCVWD, 2009).

At all three locations, soil samples (0–2 cm) were collected using Nalgene® acid-washed jars.

3.2. Laboratory methods

3.2.1. Aqueous Hg_T

For Hg_T, acidified precipitation samples were oxidized overnight with 0.5% (v/v) 0.2 N bromine monochloride (BrCl), and then pre-reduced using hydroxylamine hydrochloride. The samples were reduced further with stannous chloride ($SnCl_2$), converting inorganic Hg(II) to volatile Hg(0) (i.e., GEM), which was then purged from solution by argon gas. For Hg(II) (commonly referred to as reactive or labile Hg), samples were reduced with $SnCl_2$, leaving out the BrCl oxidation step (Hammerschmidt et al., 2007). Quantification for Hg_T and Hg(II) was by dual-stage gold amalgamation/cold vapor atomic fluorescence spectrometry (CVAFS). The oxidation–reduction steps follow established methods (Bloom and Crecelius, 1983; Bloom and Fitzgerald, 1988), which are implemented in EPA Method 1631, Revision E (USEPA, 2002).

3.2.2. Solid-phase Hg_T

Following Method 1631 Appendix for cold digestion of sediments (USEPA, 2002), ~1 g wet sediment was digested in a borosilicate glass vial overnight in 10 ml of 8:2 hydrochloric acid: nitric acid. The samples were then oxidized with 0.5 ml of 0.2 N BrCl to prevent resorption of inorganic Hg(II) to organic matter, and excess oxidant was neutralized with hydroxylamine hydrochloride. After dilution, the same procedures described for reduction and quantification of aqueous Hg_T were followed.

3.2.3. MeHg

Following addition of KCl and L-cysteine, acidified samples were distilled into receiving vials under N_2 flow using an all Teflon® system, according to methods described by Horvat et al. (1993a,b) and codified in Method 1630 (USEPA, 2001). The pH of the distillates was then adjusted to 4.9 with 2 M acetate buffer, and ethylated using 1% sodium tetraethylborate, converting nonvolatile MeHg to gaseous methylethylmercury, which was purged onto Tenax columns, then thermally desorbed from the column and quantified by CVAFS.

3.2.4. Other metals V, Ni, Pb, Sb

A modified version of EPA 1638 (USEPA, 1996) certified by the National Environmental Laboratory Accreditation Program was employed for the determination of vanadium (V), nickel (Ni), lead (Pb) and antimony (Sb), using inductively coupled plasma mass spectrometry.

3.2.5. QAQC

Detection levels for aqueous species were as follows: Hg_T (0.15 ng L^{-1}), Hg(II) (0.15 ng L^{-1}), MeHg (0.020 ng L^{-1}), V (0.03 μg L^{-1}), Ni (0.04 μg L^{-1}), Pb (0.010 μg L^{-1}), Sb (0.003 μg L^{-1}), and the detection level for solid phase Hg_T was 0.03 ng g^{-1}. The relative percent difference (RPD) between duplicate analyses were as follows: aqueous Hg_T (1.8%, $n = 13$), solid phase Hg_T (5.1%, $n = 4$), Hg (II) (11%, $n = 6$), MeHg (23%, $n = 2$), V (5.4%, $n = 2$), Ni (0%, $n = 2$), Pb (2.5%, $n = 2$), and Sb (3.1%, $n = 2$). Higher RPD for MeHg was due to one sample close to the detection level; when this sample was removed RPD was 3.6%. Average Hg_T levels for trip blanks were < MDL ($n = 6$). Average recoveries of matrix spikes and certified reference material standard were between 88% and 108% (Table 1).

All laboratory analyses were completed at Brooks Rand, LLC, located in Seattle, WA, USA.

3.3. Data for daily mass throughput at the cement plant

Data for daily mass throughput, including raw feed (tons) and petroleum coke (tons), and daily stack emissions, including SO_2 (kg) and sulfur (kg), were obtained through a Public Records request (BAAQMD, 2009). Based on throughput, the cement plant was down on the following dates: January 6–14, January 31–February 5, February 18–March 18, and March 19, which coincided partially with weeks 6, 7, 10, 12 and 16, and completely with weeks 13, 14 and 15 of this study. For correlation with Hg data, daily mass throughput and daily stack emissions were segregated by week ($n = 16$).

3.4. Data analysis

The volume weighted mean (VWM) is a descriptive statistic:

$$\text{VWM} = \frac{\sum_{i=1}^{n} (C_i V_i)}{\sum_{i=1}^{n} V_i} \quad (2)$$

where C_i is the concentration in precipitation (ng L^{-1}) for week i, V_i is the total volume (L) collected for week i, and n is the number of weeks sampled. In addition to comparing the VWM for Hg species between sites, two-tailed t-tests were calculated using un-weighted data to determine whether differences were due to chance ($p > 0.05$) or were considered significant ($p < 0.05$) (Sections 4.2 and 4.6). Aqueous Hg_T concentrations were transformed to normality using a $\log_{10}$-transformation. T-tests were not used to compare Hg_T results between the cement plant and SC Park, nor between other metals (V, Ni, Pb, Sb) measured at all three sites due to insufficient data (Sections 4.2 and 4.3). Hg_T concentrations ($\log_{10}$-transformed) measured near the cement plant were regressed on petroleum coke usage (Section 4.4) and on rain (Section 4.5). Although the sample size was small ($n = 11$), residuals from each regression model were investigated to verify standard assumptions were met (mean = 0 and constant variance). The statistics program, Stata, was used for data analysis.

4. Results and discussion

4.1. Hg_T at the cement plant

The VWM Hg_T concentration was highest near the cement plant compared to both control sites (cement plant: 13 ng L^{-1}; De Anza College: 3.4 ng L^{-1}; SC Park: 9.5 ng L^{-1}) (Table 2). Hg_T

Table 1
Average percent recovery ±1 standard deviation for matrix spikes and certified reference material (CRM), for Hg_T, MeHg, and other metals (V, Ni, Pb, Sb) in precipitation (aqueous phase) and sediments (solid phase).

	n	Matrix spike recovery (%)	n	CRM recovery (%)
Hg_T (aqueous)	36	108 ± 7.22		
Hg_T (solid)	20	104 ± 9.14	3	106 ± 3.79
MeHg (aqueous)	15	105 ± 11.5		
Hg(II) (aqueous)	4	106 ± 6.68		
V (aqueous)	5	85.4 ± 6.88	4	101 ± 7.77
Ni (aqueous)	9	91.2 ± 13.3	4	102 ± 3.20
Pb (aqueous)	9	101 ± 17.4	4	105 ± 5.80
Sb (aqueous)	1	88	4	100 ± 4.24

Table 2
Summary statistics for precipitation measured at the cement plant, De Anza College and SC Park, including average ± 1 standard deviation, range (in parentheses), sample size (n), and volume weighted mean (VWM), for Hg_T, MeHg, Hg(II), other metals (V, Ni, Pb, Sb) and summary statistics for sediment Hg_T levels.

	Cement plant	De Anza College	SC Park
Hg_T (ng L^{-1})	19 ± 19 (3.4–60) (n = 11)	4.4 ± 1.5 (2.8–6.8) (n = 6)	18 ± 13 (9.3–27) (n = 2)
Hg_T Deposition (ng m^{-2} $week^{-1}$)	320 ± 340 (17–1100) (n = 11)	110 ± 85 (6.9–230) (n = 6)	390 ± 440 (82–700) (n = 2)
Hg_T VWM (ng L^{-1})	13 (n = 11)	3.4 (n = 6)	9.5 (n = 2)
Mehg (ng L^{-1})	0.22 ± 0.18 (0.018–0.44) (n = 5)	0.38 ± 0.25 (0.21–0.56) (n = 2)	NA
MeHg Deposition (ng m^{-2} $week^{-1}$)	1.8 ± 1.7 (0.11–3.6) (n = 5)	2.9 ± 2.5 (1.1–4.7) (n = 2)	NA
MeHg VWM (ng L^{-1})	0.15 (n = 5)	0.23 (n = 2)	NA
%MeHg (of Hg_T)	2.0 ± 2.0 (0.030–4.7) (n = 5)	4.3 ± 0.67 (3.8–4.8) (n = 2)	NA
Hg(II) (ng L^{-1})	0.40 ± 0.16 (0.21–0.50) (n = 3)	0.37 ± 0.13 (0.22–0.45) (n = 3)	0.95 (n = 1)
Hg(II) Deposition (ng m^{-2} $week^{-1}$)	16 ± 6.6 (11–23) (n = 3)	16 ± 5.0 (10–20) (n = 3)	68 (n = 1)
Hg(II) VWM (ng L^{-1})	0.36 (n = 3)	0.31 (n = 3)	0.95 (n = 1)
%Hg(II) (of Hg_T)	12 ± 1.8 (11–14) (n = 3)	9.0 ± 1.5 (7.9–11) (n = 3)	12 (n = 1)
V (nM)	45 ± 56 (5.4–85) (n = 2)	6.7 ± 7.1 (1.7–12) (n = 2)	60 (n = 1)
Ni (nM)	24 ± 32 (1.0–46) (n = 2)	9.8 ± 12 (1.0–19) (n = 2)	35 (n = 1)
Pb (nM)	7.0 ± 8.8 (0.74–13) (n = 2)	3.7 ± 4.2 (0.76–6.7) (n = 2)	13 (n = 1)
Sb (nM)	0.78 ± 0.89 (0.16–1.4) (n = 2)	0.43 ± 0.32 (0.21–0.66) (n = 2)	1.4 (n = 1)
Sediments(Windward) (ng g^{-1})	95 ± 22 (80–110) (n = 2)	130 ± 19 (120–140) (n = 2)	81 ± 5.8 (77–85) (n = 2)
Sediments(Leeward) (ng g^{-1})	82 ± 34 (57–110) (n = 2)	89 ± 28 (70–110) (n = 2)	97 ± 4.5 (94–100) (n = 2)

concentrations (log_{10}-transformed) were significantly higher at the cement plant (n = 11) compared to De Anza College (n = 6) ($p < 0.05$). Elevated Hg_T levels near the cement plant occurred between weeks 1 and 9 (November 29–January 31) (VWM: 18 ng L^{-1}) (n = 7), while lowest levels occurred between weeks 10 and 16 (February 1-March 20) when cement plant operations were minimized (VWM: 4.3 ng L^{-1}) (n = 4), and this difference was significant ($p < 0.05$, Hg_T log_{10}-transformed). During week 2 (December 6–13), the cement plant was permitted to increase petroleum coke usage by 15% from 17.0 to 19.5 t h^{-1} to test compliance with emissions standards (BAAQMD, 2008); likewise, Hg_T levels in precipitation increased by 60% to their highest level (60 ng L^{-1}), despite increased volume collected (Table 3).

4.2. Hg_T comparison between the cement plant and control sites

Side-by-side data for the cement plant and De Anza College were available for weeks 8, 9, 10, 12, 13 and 16 (n = 6) (Fig. 2). The cement plant was partially or completely down during the latter four weeks (weeks 10, 12, 13, 16; no rain occurred during weeks 11, 14, and 15). During weeks 8–9, and weeks 10, 12, 13, and 16, the ratio between VWM Hg_T levels at the cement plant and De Anza College was 6.7 and 1.1, respectively (Fig. 2). For the same weeks, the ratios between average Hg_T deposition were 5.8 and 1.1, respectively, and the ratios between average Hg_T concentrations were 7.4 and 1.6, respectively. Due to the close proximity between the two sites (3.5 km apart), meteorological conditions (e.g., precipitation levels, wind direction) were similar, and therefore higher Hg_T levels when the cement plant was operational likely reflected increased Hg emissions from the cement plant. Although Hg_T deposition and concentration were higher compared to De Anza College when the cement plant was operational, t-tests were not significant (both log_{10}-transformed), which was likely due to insufficient data (n = 2 weeks prior to plant closure) ($p > 0.10$). During plant closure, differences were also not significant ($p > 0.50$, both log_{10}-transformed).

Table 3
Weekly Hg_T concentration (ng L^{-1}) and Hg_T wet deposition rates (ng m^{-2} $week^{-1}$), and weekly cement plant fuel use and stack emissions (data for cement plant from BAAQMD, 2009).

Date	Week	Cement plant		De Anza college		SC park		Cement plant mass throughput[a]		Cement plant stack emissions[a]	
2007–2008	#	Hg_T (ng L^{-1})	Hg_T deposition (ng m^{-2} $week^{-1}$)	Hg_T (ng L^{-1})	Hg_T deposition (ng m^{-2} $week^{-1}$)	Hg_T (ng L^{-1})	Hg_T deposition (ng m^{-2} $event^{-1}$)[c]	Raw feed (tons)	Petroleum coke (tons)	SO_2 (kg)	Sulfur (kg)
11/29–12/6	1	37	220					31,490	2217	2810	1405
12/6–12/13	2	60	360					42,230	2899	1874	936.7
12/13–12/20	3	8.0	210					25,040	2073	3190	1595
12/20–12/27	4[b]							25,440	2401	2004	1002
12/27–1/3	5	13	27					27,940	2311	3176	1588
1/3–1/4	6[c]	6.6	470					4350	339.3	427.3	213.6
1/10–1/17	7[b]							8376	539	518.7	259.0
1/17–1/24	8	44	790	4.9[d]	88			34,285	2196	2060	1030
1/24–1/31	9	13	1100	2.8	230			26,657	1878	3238	1618
1/31–2/7	10	3.4	77	5.3	120			3761	269.9	397.1	198.4
2/7–2/14	11[b]							30,410	2261	1779	888.4
2/14–2/21	12	4.9	78	2.8	45			12,680	904.5	857.3	404.2
2/21–2/28	13	4.6	210	4.0	180	9.3	700	0	0	0	0
2/28–3/6	14[b]							0	0	0	0
3/6–3/13	15[b]							0	0	0	0
3/13–3/20	16	17	17	6.8	6.9	27	82	783.8	56.25	64.86	32.66

[a] Daily mass throughput and daily stack emissions data from the Lehigh Hanson Cement Plant were obtained from the Bay Area Air Quality Management District Public Records request (BAAQMD, 2009).
[b] Hg data were not available for weeks 4, 7,11, 14 and 15 due to insufficient or no precipitation.
[c] Data for week 6 are for one day only (Jan 3–Jan 4).
[d] Data collection for De Anza College began during week 8 (no rain week 7).
[e] For SC Park, precipitation was collected during two events, and the Hg deposition rate was calculated per rain event (not per week).

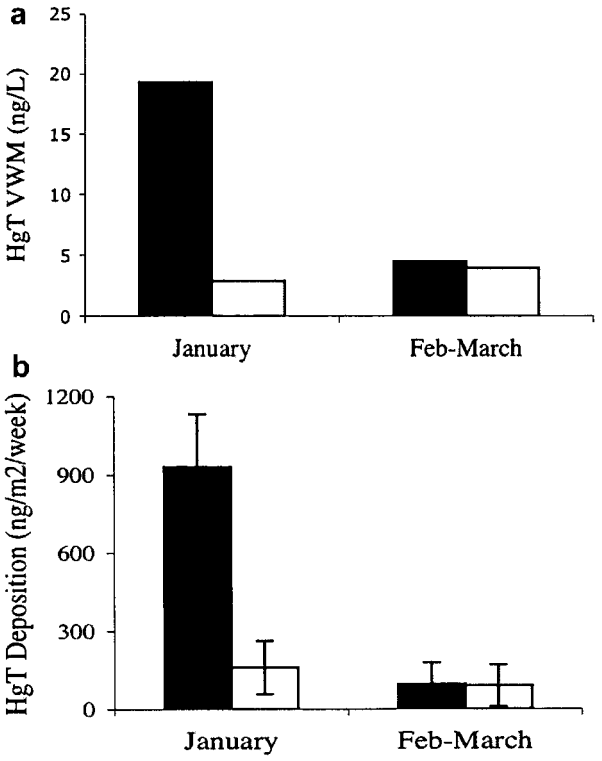


Fig. 2. Comparison between Hg_T levels at the cement plant (black bar) and the control site (De Anza College) (white bar) during January, when the cement plant was operational ($n = 2$), and during February and March ($n = 4$), when the cement plant was closed due to annual maintenance. a) Hg_T volume weighted mean (VWM) (ng L^{-1}) b) Hg_T deposition ±1 standard deviation (ng m^{-2} $week^{-1}$).

Precipitation was collected at SC Park during weeks 13 and 16 (during both weeks, cement plant operations were down). The ratio between VWM Hg_T levels and Hg_T deposition rates at the cement plant and SC Park was 0.52 and 0.24, respectively. At SC Park, Hg_T concentration and Hg_T deposition were higher than those at the cement plant (Table 3), which was unexpected considering SC Park was more isolated from Hg point sources. Elevated Hg_T levels may reflect increased Hg inputs in throughfall (Choi et al., 2008; St. Louis et al., 2001), as the sampling area was located near trees in a forested park. Particulates were also observed in the collection bottle, which were not filtered prior to analysis since acid was predispensed before deployment. Higher precipitation levels in SC Park also contributed to elevated Hg_T deposition; precipitation was 1.6 and 3.0 times higher than precipitation measured near the cement plant during weeks 13 and 16, respectively.

4.3. Other metals (V, Ni, Pb, Si)

Other metals (V, Ni, Pb, Sb) were measured during week 13 (at the cement plant and De Anza College) and week 16 (at all three sites) (Fig. 3). Both V and Ni are associated with petroleum coke emissions (Hower et al., 2005), while Pb and Sb levels typically reflect waste incineration emissions (Dvonch et al., 2005). Results from the December 10–14, 2007 cement plant compliance test showed increased emissions for all metals (e.g., Hg, V, Ni, Pb, Sb) when the hourly mass of incinerated petroleum coke was increased by 15%; metal emissions were ranked as follows (maximum g h^{-1}): Hg (10) > Ni (0.47) > V (0.25) > Pb (0.065) > Sb (0.043) (BAAQMD, 2008), which confirmed all metals were associated with incineration of petroleum coke.

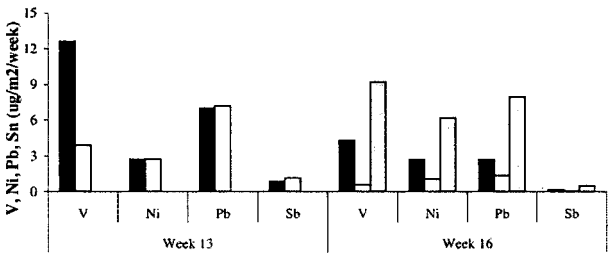


Fig. 3. Deposition of other metals (V, Ni, Pb, Sb) (μg m^{-2} $week^{-1}$) during weeks 13 and 16 at the cement plant (black bar) and two control sites (De Anza College, white bar; SC Park, gray bar). No rain occurred between weeks 13 and 16, and the cement plant was closed during both weeks. SC Park was not monitored during week 13, and during week 16 higher deposition reflected more rainfall (3 times), as concentrations for all metals were similar or lower at SC Park compared to the cement plant (Table 3).

Deposition rates were compared rather than concentrations (Fig. 3), since more rain fell during week 13 compared to week 16 (46 mm versus 1.0 mm at the cement plant and De Anza College; 76 mm versus 3.0 mm at SC Park, Table 3). There were insufficient data to calculate *t*-tests for metals at the three sites. Plant operations were minimized during week 12, and completely down from week 13 until the end of week 16 (the last week of the study). The final rain event occurred during week 16, just 4 days before cement plant operations resumed. Therefore Fig. 3 included data collected for metals only during cement plant closure.

During week 13, Ni, Pb and Sb deposition rates were similar between the cement plant and De Anza College, while V deposition was higher near the cement plant (Fig. 3). The latter suggested V may have a slightly longer atmospheric lifetime compared to the other metals, or V was more concentrated near the cement plant and may take longer to attenuate. V may also have a higher affinity for particulates. During week 16, after nearly 4 weeks of no plant operations and 20 days since the previous rain event, deposition for all metals decreased near the cement plant and De Anza College. However unlike week 13, deposition rates for all metals were higher at the cement plant during week 16, which may be due to more sustained particulates near the cement plant.

During week 16, other metals were also measured at SC Park, where deposition was higher compared to the cement plant and De Anza College (Fig. 3). Concentrations for all metals were lower at SC Park compared to the cement plant, but higher than those measured at the De Anza College. Precipitation was 3 times higher at SC Park compared to the other two sites (see Section 4.2), which resulted in higher deposition.

4.4. Correlation between Hg_T, fuel use, raw feed and sulfur emissions

Assuming no hazardous materials are used as fuel, the primary sources of Hg emissions from portland cement processing include combustion of fossil fuels (e.g., petroleum coke) and incineration of raw materials (e.g., limestone) at high temperatures (i.e., 350 °C) (USEPA, 1997). Raw materials and petroleum coke were highly correlated ($r^2 = 0.97$, $p < 0.001$, $n = 15$, data from BAAQMD, 2009), and both were positively associated with Hg_T concentrations in precipitation, although raw materials were more highly correlated ($\log_{10}$ Hg_T versus raw materials: $r^2 = 0.65$; $\log_{10}$ Hg_T versus coke: $r^2 = 0.58$, $p < 0.05$ for both). The associations between the Hg_T deposition rate (ng m^{-2} $week^{-1}$) and raw materials and petroleum coke were weaker ($\log_{10}$ Hg_T deposition versus raw feed: $r^2 = 0.15$; $\log_{10}$ Hg_T deposition versus coke: $r^2 = 0.20$, $p > 0.10$ for both), indicating rain does not

effectively washout Hg near the cement plant (discussed further in Section 4.5).

Raw materials and fuel both contribute to Hg emissions; however the air quality permit is based primarily on fuel consumption. For regulatory purposes, the following regression model may provide information on the consequences of increasing petroleum coke on Hg_T levels in precipitation, when petroleum coke is the sole fuel used (see Fig. 4):

$$\log_{10} Hg_T = 0.69 + 0.29 \text{petroleum coke}/1000\text{t} \quad (r^2 = 0.58, p < 0.05) \quad (3)$$

A regression equation in which the dependent variable is $\log_{10}$-transformed may be interpreted as follows: for a 1000 t weekly increase in petroleum coke usage, the average Hg_T concentration in precipitation (ng L^{-1}) near the cement plant is expected to increase by 95% ($=100 \times (10^{0.29 \times 1.00} - 1)$). In 2008, the cement plant applied for a permit to increase petroleum coke usage by 33% from 18 to 24 t h^{-1} ($=1.008 \times 1000$ additional t coke $week^{-1}$), but withdrew the request (Brian Bateman, BAAQMD, personal communication). From the regression model, this increase may lead to a 96% increase in the average Hg_T level in precipitation ($=100 \times (10^{(0.29 \times 1.008)} - 1)$). Due to the low sample size ($n = 11$), more observations are needed to verify this relationship.

Hg_T levels in precipitation ($\log_{10}$-transformed) were not well correlated with sulfur levels measured in stack emissions ($r^2 = 0.25$, $p > 0.05$). This was possibly due to technology designed to remove sulfur but not Hg, or may reflect variability in Hg species emitted. For European cement plants, the estimated proportion of Hg species is: 80% gaseous elemental Hg (GEM), 17% reactive gaseous Hg (i.e., RGM or Hg(II)), and 3% particulate-bound (Hg_p) (Pacyna et al., 2006). GEM, RGM and Hg_p were monitored in 2007 and 2008 near the cement plant and intermittent peaks were observed (Rothenberg et al., in press). It is likely the proportion of each Hg species was not constant during the 16-week study, which increased the variability between sulfur levels and precipitation Hg_T levels.

4.5. Washout effect and the scavenging ratio

Two relationships are used to investigate the importance of scavenging of Hg_T by rainfall: the washout effect and the scavenging (or washout) ratio (Guentzel et al., 1995; Lamborg et al., 1995; Lynam and Gustin, 2008; Mason et al., 1997; Steding and Flegal, 2002). The washout effect is characterized by a negative correlation between Hg_T concentrations and rainfall, and indicates dilution and rapid washout of Hg_T. An inverse correlation was observed between Hg_T levels ($\log_{10}$-transformed) and precipitation near the cement plant and De Anza College, although relationships at both sites were not significant (cement plant: $r^2 = 0.15$, $p > 0.05$; De Anza College: $r^2 = 0.43$, $p > 0.05$). A stronger correlation indicates proximity to a source, while a lack of correlation suggests non-local sources may be important (Steding and Flegal, 2002). Therefore, it is interesting to note an inverse correlation was stronger at De Anza College, located 3.5 km east of the cement plant. It is possible Hg_T concentrations were more sustained near the cement plant, similar to V, which was not diminished over time like other metals (see Section 4.3). For both sites, the sample size was small (cement plant: $n = 11$, De Anza College: $n = 6$), and therefore regression results were likely biased.

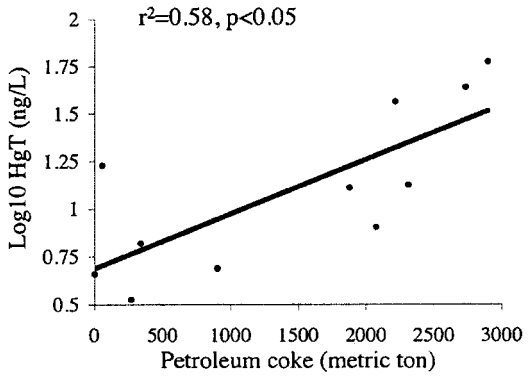


Fig. 4. Regression between $\log_{10}$ Hg_T concentrations (ng L^{-1}) in precipitation versus petroleum coke (t) ($r^2 = 0.58$, $p < 0.05$). Data for daily fuel usage obtained from a Public Records request to the Bay Area Air Quality Management District (BAAQMD, 2009).

The scavenging ratio (S, unitless) is defined as the mass of a substance (e.g., Hg) per unit mass of rain or air (Duce et al., 1991):

$$S = \frac{Hg_{rain} \times \rho_{atm}}{Hg_p \times \rho_{rain}} \quad (4)$$

where $[Hg_{rain}]$ = concentration of Hg_T in precipitation (ng L^{-1}), $\rho_{atm} = 1.2$ kg m^{-3}, $[Hg_p]$ = the concentration of particulate Hg (Hg_p) in the atmosphere (ng m^{-3}) and $\rho_{rain} = 1$ kg L^{-1}. RGM was also water-soluble (Schroeder and Munthe, 1998), and therefore the scavenging ratio was calculated using the sum of Hg_p + RGM. Atmospheric Hg levels (including Hg_p and RGM) were monitored at the same location near the cement plant November 26–December 12, 2007 (17 days) using an automated Tekran 2537A/1130/1135 speciation unit (Landis et al., 2002) (Rothenberg et al., in press), and overlapped precipitation collection during week 1 and the first six days of week 2 (November 29–December 6, December 6–12). During the 17-day deployment, Hg_p + RGM averaged 38 pg m^{-3}.

Values between 200 and 2000 for other metals are considered typical in areas where scavenging of particles is an important process (Duce et al., 1991). When the cement plant was operational the scavenging ratio was 820 ± 660, and during plant closure the ratio was 240 ± 200. When the data for all weeks were combined, the scavenging ratio was 600 ± 600 (range: 100–1900). Lower values during cement plant closure were due to reduced Hg_T concentrations in precipitation (Section 4.1). When the cement plant was operational, the values for the scavenging ratio were considered elevated compared to those measured in Wisconsin (477 ± 547 and 181 ± 129, from Lamborg et al., 1995), while the average (i.e., 820) was lower compared to the Chesapeake Bay (average = 1110, from Mason et al., 1997), and lower than those observed in Florida near the Everglades (winter: 2000–3000, summer: 3000–6000, from Guentzel et al., 1995). Lower scavenging values likely reflected higher Hg_p + RGM levels due to proximity to the cement plant (this study: 38 pg m^{-3}, Chesapeake Bay: 18 pg m^{-3}, from Mason et al., 1997; Florida 1.5–12.8 pg m^{-3}, from Guentzel et al., 1995; Wisconsin: winter: 7 pg m^{-3}, summer 26 pg m^{-3}, from Lamborg et al., 1995).

4.6. Comparison with mercury deposition network dataset

In 2007, data pooled from over 85 Mercury Deposition Network (MDN) sites in the USA defined maximum Hg_T levels in precipitation as greater than 18 ng L^{-1} (MDN, 2009). MDN sites are typically located away from point sources to capture background levels of Hg_T. Therefore, it was not surprising the average Hg_T level near the cement plant during weeks 1–9 (when the cement plant was operational) was greater than 18 ng L^{-1} (average: 26 ng L^{-1}), while the average Hg_T level during weeks 10–16 (when the cement plant was down) was 7.4 ng L^{-1}, which corresponded to the third lowest category (6–8 ng L^{-1} from MDN, 2009); i.e., similar to other background sites.

Between January 2000 and December 2006, the MDN network included Moffett Field (site # CA72; from MDN, 2009), located 11 km northeast of the cement plant. Total Hg_T deposition at the cement plant between November 29, 2007 and March 20, 2008 was 3.5 μg m^{-2}. At Moffett Field, during the same 4-month period in previous years, total Hg_T deposition was 1.5 μg m^{-2} (2001–2002), 1.0 μg m^{-2} (2002–2003), 1.5 μg m^{-2} (2003–2004), 1.3 μg m^{-2} (2004–2005), and 2.5 μg m^{-2} (2005–2006). When the cement plant was operational (weeks 1–9), Hg_T deposition (log_{10}-transformed) was significantly higher compared to levels measured at Moffett Field for the corresponding weeks in 2000–2001, 2002–2003, 2004–2005 ($p < 0.05$), while Hg_T concentrations (log_{10}-transformed) were significantly higher compared to levels measured at Moffett Field during the same timeframe in 2002–2003, 2004–2005, 2005–2006 ($p < 0.05$). When the cement plant was not fully operational (weeks 10–16), Hg_T deposition and Hg_T concentration (both log_{10}-transformed) were similar to those measured at Moffett Field for the same weeks for all six years ($p > 0.05$); i.e., the cement plant was similar to a background site.

4.7. MeHg and reactive Hg levels in precipitation

MeHg was measured in precipitation at the cement plant (weeks 2, 3, 5, 9, 10) and one control site (De Anza College) (weeks 9, 10). At the cement plant, the ratio between the MeHg VWM between weeks when the cement plant was fully operational and when the cement plant was down was 0.92, indicating no effect to MeHg levels from cement plant operations. MeHg levels at the cement plant were not significantly higher than those measured at De Anza College ($p > 0.05$). During weeks 9–10, the ratio between the MeHg VWM at both sites was 0.75, which indicated slightly higher MeHg levels at the control site. Munthe et al. (2003) measured Hg species directly in the stacks of several European power plants and waste incinerators, and reported emissions of MeHg were insignificant in all stack gases although other Hg species varied. Results from this study were in agreement, i.e., cement plant emissions were not a significant source of MeHg to the atmosphere during this sampling period.

Hg(II) was measured at the cement plant and De Anza College (weeks 9, 10, 13) and at SC Park (week 13). During this time, the cement plant was down partially during week 10 and completely down during week 13. The ratio of Hg(II) VWM between the cement plant and De Anza College for weeks 9, 10, and 13 was 1.2; when only weeks 10 and 13 were compared (when the cement plant was down), the ratio was 1.1 ($p > 0.05$). Hg(II) was measured at SC Park in precipitation collected during week 13; the Hg(II) VWM ratio between the cement plant ($n = 3$) and SC Park ($n = 1$) was 0.38. Although Hg(II) was measured in fewer samples, results suggested the portion of Hg considered more labile (i.e., more reactive) was similar between the cement plant and De Anza College.

4.8. Comparison of soil Hg_T levels between three sites

Soils (0–2 cm) were collected at two locations within all three sites, one less obstructed (windward side) and one more protected (leeward side) (Table 2). No significant differences were observed between Hg_T levels from the windward and leeward sites, nor among the three sites ($p > 0.50$). Average Hg_T soil levels from all three sites were lower than sediment Hg_T levels for a study of 26 sites throughout the San Francisco Bay (average: 96 ± 18 ng g^{-1} from this study; average: 200 ng g^{-1}, Conaway et al., 2003), and only 5/12 observations were considered contaminated (i.e., >100 ng g^{-1}). Higher Hg_T levels in the San Francisco Bay reflected elevated inputs from atmospheric sources as well as historical mining and wastewater runoff (Conaway et al., 2003; Flegal et al., 2005), while soils for this study were from upland sites and Hg_T levels likely reflected atmospheric inputs. Comparable Hg_T soil levels across all three sites suggested soils were washed into the Bay through storm water runoff, which was reported for other regions of the estuary (Conaway et al., 2007). Greater spatial sampling is needed to characterize the distribution of soil Hg levels, especially near the cement plant.

5. Conclusions

Hg emissions from the cement plant do not all enter the global circulation cycle and undergo long-range transport; Hg is also deposited within the vicinity of the cement plant through wet deposition. During cement plant closure, the VWM for Hg_T was reduced by a factor of 4.2. When the cement plant was not operational, Hg_T wet deposition rates and Hg_T concentrations in precipitation were similar to those measured at background sites, including a nearby control site (3.5 km east of the cement plant, De Anza College), other sites dispersed nationally in the MDN network, and historically at Moffett Field (11 km northeast of the cement plant), while Hg_T concentrations were significantly higher during normal operations at the cement plant ($p < 0.05$). From this study, it was not possible to determine whether fuel use or raw feed (i.e., limestone) was the predominant Hg source. However, due to the strong correlation between the two ($r^2 = 0.97$), lower fuel use would likely translate into lower use of raw materials. Although data were collected for only one rainy season, results from this study suggested a reduction in cement plant operations (i.e., lower fuel use) would lead to a corresponding decrease in Hg_T deposition to the surrounding community.

Acknowledgements

The authors wish to thank Chris Sommers (BAASMA), Geoff Brosseau (BAASMA), and Richard Looker (SFRWQCB) for their helpful advice, as well as the comments from two anonymous reviewers whose suggestions greatly enhanced the manuscript. The authors also thank Pat Cornely and Prof. Julie Phillips for permission to sample at De Anza College. This study was funded through California Proposition 13 (Costa-Machado Water Act, 2000). S. Rothenberg was supported by the NSF International Research Fellowship Program (Grant # 0802014), and both S. Rothenberg and X. Fu were supported by the State Key Laboratory of Environmental Geochemistry, Institute of Geochemistry, Chinese Academy of Sciences in Guiyang, China.

References

Bay Area Air Quality Management District (BAAQMD), 2008. Source Test Report 2007 Emissions Compliance Tests, Hanson Permanente Cement, Cupertino, California. In: Prepared for Hanson Permanente Cement by John S. Peterson, The Avogadro Group, LLC, 11.02.08, 78 pp.

Bay Area Air Quality Management District (BAAQMD), 2009. Public Records request, www.baaqmd.gov/Divisions/Legal/Public-Records-Request.aspx (Cited August 2009).

Bloom, N.S., Crecelius, E.A., 1983. Determination of mercury in seawater at sub-nanogram per liter levels. Marine Chemistry 14, 49–59.

Bloom, N.S., Fitzgerald, W.F., 1988. Determination of volatile mercury species at the picogram level by low temperature gas chromatography with cold vapor atomic fluorescence detection. Analytica Chimica Acta 208, 151–161.

California Air Resources Board (CARB), 2009. Facility Search Results. www.arb.ca.gov/app/emsinv/facinfo/facinfo.php (Cited August 2009).

Choi, H.-D., Sharac, T.J., Holsen, T.M., 2008. Mercury deposition in the Adirondacks: a comparison between precipitation and throughfall. Atmospheric Environment 42, 1818–1827.

Conaway, C.H., Squire, S., Mason, R.P., Flegal, A.R., 2003. Mercury speciation in the San Francisco estuary. Marine Chemistry 80, 199–225.

Conaway, C.H., Watson, E.B., Flanders, J.R., Flegal, A.R., 2004. Mercury deposition in a tidal marsh of south San Francisco Bay downstream of the historic New Almaden mining district, California. Marine Chemistry 90, 175–184.

Conaway, C.H., Ross, J.R.M., Looker, R., Mason, R.P., Flegal, A.R., 2007. Decadal mercury trends in San Francisco Estuary sediments. Environmental Research 105, 53–66.

Duce, R.A., Liss, P.S., Merrill, J.T., Atlas, E.L., Buat-Menard, P., Hicks, B.B., Miller, J.M., Prospero, J.M., Arimoto, R., Church, J.M., Ellis, W., Galloway, J.N., Hansen, L., Jickells, T.D., Knap, A.H., Reinhardt, K.H., Schneider, B., Soudine, A., Tokos, J.J., Tsunogai, S., Wollast, R., Zhou, M., 1991. The atmospheric input of trace species to the world ocean. Global Biogeochemical Cycles 5, 193–259.

Dvonch, J.T., Keeler, G.J., Marsik, F.J., 2005. The influence of meteorological conditions on the wet deposition of mercury in southern Florida. Journal of Applied Meteorology 44, 1421–1435.

Flegal, A.R., Conaway, C.H., Scelfo, G.M., Hibdon, S.A., Sanudo-Wilhelmy, S.A., 2005. A review of factors influencing measurements of decadal variations in metal contamination in San Francisco Bay, California. Ecotoxicology 14, 645–660.

Guentzel, J.L., Landing, W.M., Gill, G.A., Pollman, C.D., 1995. Atmospheric deposition of mercury in Florida: the FAMS project (1992–1994). Water Air and Soil Pollution 80, 393–402.

Hammerschmidt, C.R., Fitzgerald, W.F., 2006. Methylmercury in freshwater fish linked to atmospheric mercury deposition. Environmental Science and Technology 40, 7764–7770.

Hammerschmidt, C.R., Lamborg, C.H., Fitzgerald, W.F., 2007. Aqueous phase methylation as a potential source of methylmercury in wet deposition. Atmospheric Environment 41, 1663–1668.

Harris, R.C., Rudd, J.W.M., Amyot, M., Babiarz, C.L., Beaty, K.G., Blanchfield, P.J., Bodaly, R.A., Branfireun, B.A., Gilmour, C.C., Graydon, J.A., Heyes, A., Hintelmann, H., Hurley, J.P., Kelly, C.A., Krabbenhoft, D.P., Lindberg, S.E., Mason, R. P., Paterson, M.J., Podemski, C.L., Robinson, A., Sandilands, K.A., Southworth, G.R., St. Louis, V.L., Tate, M.T., 2007. Whole-ecosystem study shows rapid fish-mercury response to changes in mercury deposition. Proceedings of the National Academy of Sciences 104, 16586–16591.

Hintelmann, H., Harris, R., Heyes, A., Hurley, J.P., Kelly, C.A., Krabbenhoft, D.P., Lindberg, S., Rudd, J.W.M., Scott, K.J., St. Louis, V.L., 2002. Reactivity and mobility of new and old mercury deposition in a boreal forest ecosystem during the first year of the MEAALICUS study. Environmental Science and Technology 36, 5034–5040.

Horvat, M., Bloom, N.S., Liang, L., 1993a. Comparison of distillation with other current isolation methods for the determination of methyl mercury compounds in low level environmental samples, part 1, sediments. Analytica Chimica Acta 281, 135–152.

Horvat, M., Bloom, N.S., Liang, L., 1993b. Comparison of distillation with other current isolation methods for the determination of methyl mercury compounds in low level environmental samples, part 2, water. Analytica Chimica Acta 282, 153–168.

Hower, J.C., Thomas, G.A., Mardon, S.M., Trimble, A.S., 2005. Impact of co-combustion of petroleum coke and coal on fly ash quality: case study of a western Kentucky power plant. Applied Geochemistry 20, 1309–1319.

Lamborg, C.H., Fitzgerald, W.F., Vandal, G.M., Rolfhus, K.R., 1995. Atmospheric mercury in northern Wisconsin: sources and species. Water Air and Soil Pollution 80, 189–198.

Landis, M.S., Stevens, R.K., Schaedlich, F., Prestbo, E.M., 2002. Development and characterization of annular denuder methodology for the measurement of divalent inorganic reactive gaseous mercury in ambient air. Environmental Science and Technology 36, 3000–3009.

Lynam, S.N., Gustin, M.S., 2008. Speciation of atmospheric mercury at two sites in northern Nevada, USA. Atmospheric Environment 42, 927–939.

Mason, R.P., Lawson, N.M., Sullivan, K.A., 1997. The concentration, speciation and sources of mercury in Chesapeake Bay precipitation. Atmospheric Environment 31, 3541–3550.

Mercury Deposition Network (MDN), 2009. Mercury Deposition Network: a NADP Network. http://nadp.sws.uiuc.edu/mdn/ (Cited August 2009).

Minnesota Pollution Control Agency (MPCA), 2008. Minnesota Statewide Mercury TMDL. http://www.pca.state.mn.us/water/tmdl/tmdl-mercuryplan.html (Cited August 2009).

Munthe, J., Wangberg, I., Iverfeldt, A., Lindqvist, O., Stromberg, D., Sommar, J., Gardfeldt, K., Peterson, G., Ebinghaus, R., Prestbo, E., Larjava, K., Siemens, V., 2003. Distribution of atmospheric mercury species in Northern Europe: final results from the MOE project. Atmospheric Environment 37, S9–S20.

New England Interstate Water Pollution Control Commission (NEIWPCC), 2008. Northeast Regional Mercury TMDL. http://www.neiwpcc.org/mercury/MercuryTMDL.asp (Cited August 2009).

Pacyna, E.G., Pacyna, J.M., Fudala, J., Strzelecka-Jastrzab, E., Hlawiczka, S., Panasiuk, D., 2006. Mercury emissions to the atmosphere from anthropogenic sources in Europe in 2000 and their scenarios until 2020. Science of the Total Environment 370, 147–156.

Rothenberg, S.E., McKee, L., Gilbreath, A., Yee, D., Conner, M., Fu, X. Evidence for short range transport of atmospheric mercury to a rural, inland site, Atmospheric Environment, in press. doi:10.1016/j.atmosenv.2009.12.032.

St. Louis, V.L., Rudd, J.W.M., Kelly, C.A., Hall, B.D., Rolfhus, K.R., Scott, K.J., Lindberg, S.E., Dong, W., 2001. Importance of the forest canopy to fluxes of methyl mercury and total mercury to boreal ecosystems. Environmental Science and Technology 35, 3089–3098.

Santa Clara Valley Water District (SCVWD), 2009. Santa Clara Valley Water District ALERT Gage System. http://alert.scvwd.org (Cited August 2009).

Schroeder, W., Munthe, J., 1998. Atmospheric mercury – an overview. Atmospheric Environment 32, 809–822.

Steding, D.J., Flegal, A.R., 2002. Mercury concentrations in coastal California precipitation: evidence of local and trans-Pacific fluxes of mercury to North America. Journal of Geophysical Research 107, 4764. doi:10.1029/2002JD002081.

U.S. EPA. (USEPA), 1996. Method 1638, Determination of Trace Elements in Ambient Waters by Inductively Coupled Plasma-mass Spectrometry. USEPA, Washington, D.C.

U.S. EPA (USEPA), 1997. Mercury study report to Congress. EPA-452/R-97-003.

U.S. EPA. (USEPA), 2001. Method 1630, Methyl Mercury in Water by Distillation, Aqueous Ethylation, Purge and Trap, and Cold Vapor Atomic Spectrometry. USEPA, Washington, D.C.

U.S. EPA. (USEPA), 2002. Method 1631, Revision E: Mercury in Water by Oxidation, Purge and Trap, and Cold Vapor Atomic Fluorescence Spectrometry. USEPA, Washington, DC.

U.S. E.P.A. (USEPA), 2008. Listing Waters Impaired by Atmospheric Mercury under Clean Water Act Section 303(d) Memorandum, March 27, 2008. http://www.epa.gov/owow/tmdl/mercury5m/ (Cited August 2009).

U.S. E.P.A. (USEPA), 2009. Impaired Waters and Total Maximum Daily Loads. http://www.epa.gov/owow/tmdl (Cited August 2009).

Western Region Climate Center (WRCC), 2009. Wind Rose Plots for La Honda, CA. Obtained from. http://www.raws.dri.edu/wraws/ccaF.html (Cited August 2009).

World Health Organization (WHO), 1990. Environmental Health Criteria. In: Methylmercury, vol. 101. World Health Organization, Geneva. 1990.

World Health Organization (WHO), 1991. Environmental Health Criteria. In: Inorganic Mercury, vol. 118. World Health Organization, Geneva. 1991.

EXHIBIT 4

ELSEVIER

Health & Place ▮ (▮▮▮▮) ▮▮▮–▮▮▮

HEALTH & PLACE

www.elsevier.com/locate/healthplace

Proximity to point sources of environmental mercury release as a predictor of autism prevalence

Raymond F. Palmer[a,*], Stephen Blanchard[b], Robert Wood[a]

[a]*University of Texas Health Science Center, San Antonio Department of Family and Community Medicine, 7703 Floyd Curl Drive, San Antonio Texas, Mail Code 7794, TX 78229-3900, USA*

[b]*Department of Sociology, Our Lady of the Lake University, San Antonio Texas, TX, USA*

Received 2 October 2006; received in revised form 16 January 2008; accepted 4 February 2008

Abstract

The objective of this study was to determine if proximity to sources of mercury pollution in 1998 were related to autism prevalence in 2002. Autism count data from the Texas Educational Agency and environmental mercury release data from the Environmental Protection Agency were used. We found that for every 1000 pounds of industrial release, there was a corresponding 2.6% increase in autism rates ($p<.05$) and a 3.7% increase associated with power plant emissions($P<.05$). Distances to these sources were independent predictors after adjustment for relevant covariates. For every 10 miles from industrial or power plant sources, there was an associated decreased autism Incident Risk of 2.0% and 1.4%, respectively ($p<.05$). While design limitations preclude interpretation of individual risk, further investigations of environmental risks to child development issues are warranted.

Keywords: Mercury; Autism; Environment; Distance; Industry

Introduction

Mercury is a heavy metal found naturally in trace amounts in the earth's atmosphere in differing forms—as elemental vapor, reactive gaseous compounds, or particulate matter. Studies show that background levels of environmental mercury deposition have steadily increased several fold since the pre-industrial era (Schuster et al., 2002), with the largest source of potentially adverse exposures coming primarily from coal-fired utility plants (33%), municipal/medical waste incinerators (29%) and commercial/industrial boilers (18%)—estimated to be responsible for 158 tons of environmental mercury released per year in the US (Environmental Protection Agency, Report to Congress, 1997). Other sources include hazardous waste sites, cement factories, and chlorine production plants. According to the Agency for Toxic Substances and Disease Registry (ATSDR), next to arsenic and lead, mercury is the third most frequently found toxic substance in waste facilities in the United States (ATSDR, 2001).

Mercury is now widespread in the environment (EPA, 1997; ATSDR, 2001). The long-range atmospheric transport of mercury (Ebinghaus et al., 2001), and its conversion to organic forms through bio-accumulation in the aquatic food chain has been known for some time (MacGregor, 1975; Mahaffey, 1999). Notwithstanding, there are emerging concerns over the potential adverse effects of ambient levels of environmental mercury during early childhood development. There is sufficient evidence that children and other developing organisms are particularly susceptible to the adverse neurological effects of mercury (Landrigan and Garg, 2002; Grandjean et al., 1995; Ramirez et al., 2003; Rice and Barone, 2000).

Evidence from animal studies suggests that neonates lack the ability to efficiently excrete both methylmercury (Rowland et al., 1983) and inorganic mercury (Thomas and Smith, 1979), and that there is a higher lactational transfer of inorganic mercury than methylmercury (Sundberg et al., 1991a, b). Correspondingly, it has been shown that infants exposed via milk from mothers who were accidentally

*Corresponding author. Tel.: +1 210 827 7681.
E-mail address: palmerr@uthscsa.edu (R.F. Palmer).

1353-8292/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.healthplace.2008.02.001

Please cite this article as: Palmer, R.F., et al., Proximity to point sources of environmental mercury release as a predictor of autism prevalence. Health & Place (2008), doi:10.1016/j.healthplace.2008.02.001

poisoned by methylmercury-contaminated bread in Iraq accumulated higher mercury concentrations in their blood than did their mothers (Amin-Zaki et al., 1988) and the Faroe Island studies show that hair mercury concentrations in infants increased with the duration of the nursing period (Grandjean et al., 1994). It has also been shown that maternal dental amalgams have been linked to higher body burdens in infants (Oskarsson et al., 1996).

A 10-year longitudinal cohort monitoring study in Finland demonstrated that median hair total mercury concentrations increased in individuals who lived 2 km from a mercury polluting power plant compared to unexposed reference groups living further away (Kurttio et al., 1998). A study performed in China demonstrated that higher mercury concentrations are present in soil sediments and rice fields that are in close proximity to mercury emitting industrial plants and mining operations compared to areas that are more distant (Wang et al., 2003). A variety of similar investigations involving human, plant, and animal studies performed in different global locations consistently demonstrate that mercury concentrations are inversely associated with distance to the environmental source (Ordonez et al., 2003; Fernandez et al., 2000; Hardaway et al., 2002; Navarro et al., 1993; Kalac et al., 1991; Moore and Sutherland, 1981).

A 2000 report by the National Academy of Sciences' National Research Council estimates that approximately 60,000 children per year may be born in the US with neurological problems due to in utero exposure to methylmercury (NAS, 2000). The neurotoxicity of low-level mercury exposure has only recently been documented (NAS, 2000; EPA, 1997) and little is known about persistent low-dose ambient exposures coming from environmental sources or its influence on childhood developmental disorders such as autism—a condition affecting impairments in social, communicative, and behavior development typically present before age 3 years manifested by abnormalities in cognitive functioning, learning, attention, and sensory processing (Yeargin-Allsopp et al., 2003; CDC, 2007).

One hypothesis, which has been advanced to explain the recently observed increases in autism in the US and Europe, is that biological damage from neurotoxic substances such as mercury may play a causal role (Bernard et al., 2002). Holmes et al. (2003) found that mercury levels in the hair of autistic children were significantly lower than non-autistic controls indicating, according to the authors, that autistic children retain mercury in their body due to impairments in detoxification pathways. After the administration of a heavy metal chelating agent, Bradstreet et al. (2003) demonstrated that autistic children, relative to controls excreted more mercury in urine than non-autistic controls. Two recent studies have shown that body burden of mercury, as indicated by increased levels of urinary porphyrins specific to mercury exposure, are significantly higher in autistic children than in non-autistic children (Nataf et al., 2006; Geier and Geier, 2006).

While the association between autism and thimerisol (a mercury-based preservative formerly used in the childhood vaccination schedule during the 1990s) has not been scientifically established (Freed et al., 2002; Schechter and Grether, 2008), two studies have demonstrated an association with environmental sources of mercury and autism. Windham et al. (2006) demonstrated that ambient air mercury was associated with elevated autism risk in a case–control study in California, and Palmer et al. (2006) demonstrated that environmental mercury pollution was associated with point prevalence estimates of autism using EPA reported mercury release data from 254 counties in Texas. A major limitation to this study was that the cross-sectional design precluded any causal inferences. In addition, exposure was inferred from total pounds of environmentally released mercury aggregated at the county level at a specific point in time. Using distance to potential exposure sources may be a more reasonable proxy for exposure than one defined by total amount contained within artificial county boundaries. Given the literature on the relevance of proximity to the source of mercury and body burden, we suspect that distance to the source of mercury exposure may actually explain, at least in part, the association between increased autism rates and environmental mercury pollution found in both the Palmer et al. (2006) and Windham et al. (2006) studies.

The objective of the current study is to determine if proximity to major sources of mercury pollution is related to autism prevalence rates.

Methods

Data source and sample

Data for environmentally released mercury were obtained from the *United State Environmental Protection Agency Toxics Release Inventory* (TRI) (USEPA-TRI, 2006). TRI collects information about chemical releases and waste management reported by major industrial facilities in the US. The TRI database was established by Section 313 of the Emergency Planning and Community Right-To-Know Act of 1986 (EPCRA). Under EPCRA, industrial facilities in specific sectors are required to report their environmental releases and waste management practices annually to the EPA. Facilities covered by this act must disclose their releases to air, water, and land of approximately 650 toxic chemicals, as well as the quantities of chemicals they recycle, treat, burn, or otherwise dispose of on-site and off-site. The current analysis used the 1998 county pollution report that industrial facilities provided to TRI. Data for environmentally released mercury by coal-fired power plants were obtained from TRI and from the Texas Commission for Environmental Quality. In all, 39 coal-fired power plants and 56 industrial facilities in Texas were used in the analysis.

Please cite this article as: Palmer, R.F., et al., Proximity to point sources of environmental mercury release as a predictor of autism prevalence. Health & Place (2008), doi:10.1016/j.healthplace.2008.02.001

Measure of distance from mercury sources

The address location of coal-fired power plants and industrial facilities were entered into Arc-view V 9.0 Geographic Information Systems software along with polygonal shapes or boundaries of the school districts of Texas. GIS was then used to assign the *XY* location coordinates (latitude and longitude) of each plant and facility as well as to locate the centroid or *XY* geographical center of each school district. The amount of mercury emitted by each plant and by each facility was weighted on the *XY* coordinate of each plant's and facility's location. Using SPSS version 14 software, the distances between the *XY* coordinate of each source of emission and the *XY* coordinate of each school district centroid were calculated. As a result, each school district received a distance-in-miles measurement calculated separately for power plants and industrial facilities.

School district data

Administrative data from the Texas Education Agency (TEA) were analyzed. In compliance with the Texas Education Code, the Public Education Information Management System (PEIMS) contains data necessary for the legislature and the TEA to perform their legally authorized functions in overseeing public education. The database consists of student demographic, personnel, financial, and organizational information. Data descriptions are available at the TEA website http://www.tea.state.tx.us/data.html. Autism counts per school district were obtained by special request from the TEA. Data were from 1040 school districts in 254 counties in Texas. Diagnoses of autistic disorder are abstracted from the school records and are made by qualified special education psychologists employed by the TEA or from psychologists or medical doctors outside the TEA system. While diagnoses were not standardized, there is considerable evidence that diagnoses of autistic disorder are made with good reliability and specificity in the field (Eisenmajer et al., 1996; Hill et al., 2001; Mahoney et al., 1998). Autism prevalence rates from 2002 were used as the outcome and 1997 rates were used as a covariate in multivariate regression models.

We have identified the key covariates from prior work (Palmer et al., 2005, 2006), which were used in this study to adjust for potential confounding. *Urbanicity* and *School District Resources* have been demonstrated to be important covariates as they relate to greater identification of autism spectrum disorders. We also include a measure of ethnicity (percent white in school district).

Urbanicity

Eight separate demographically defined school district regions were used in the analysis as defined by the TEA: major urban districts and other central cities (1) major suburban districts and other central city suburbs (2) non-metropolitan and rural school districts (5).

In the current analysis, dummy variables were included in the analysis coding urban (dummy variable 1, and suburban (dummy variable 2), contrasted with non-metro and rural districts which were the referent group. Details and specific definitions of urbanicity categories can be obtained at the TEA website http://www.tea.state.tx.us/data.html.

Racial composition was accounted for by the proportion of White children enrolled in schools within each district.

Total number of students reflects all enrolled students in the districts 2002 school year and was used as the denominator in calculating autism rates.

District population wealth was calculated as the district's total taxable property value in 1998 as determined by the Comptroller's Property Tax Division (CPTD), divided by the total number of students in the district in 1998. Property value was determined by the CPTD as part of its annual study, which attempts to present uniformly appraised property valuations statewide. The CPTD value is calculated by applying ratios created from uniform independent appraisals to the district's assessed valuations.

Statistical methods

District autism data in 2002 were treated as event counts and used as the outcome in a Poisson regression model predicted by pounds of environmental mercury release in 1998, distance to sources of the release, and the relevant covariates. Total number of students enrolled in each district for 2002 defined the rates for each district. An over dispersion correction was applied due to the mean and variance not being equal. Due to the hierarchical structure of the data (e.g. districts nested within counties), the Poisson model was fit using MlWin multilevel modeling software (Rasbash et al., 1999) to obtain unbiased standard errors. Polynomials were added to the model to determine if a non-linear association was present between pounds of mercury, distance and autism rates. Regression coefficients of the models are reported as incident rate ratios by exponentiating the Poisson model coefficients.

Modeling strategy

Pounds of mercury release were first entered into the model followed by polynomial functions to access non-linear associations with autism rates. Next, *distance* was entered into the model to determine if it decreased the effect of *pounds*. Finally all covariates were entered: baseline *autism rates in 1997*, *urbanicity*, *racial composition*, *proportion of economically disadvantaged students,* and *district population wealth.* Note that mercury release data from 1998 are used to predict autism rates in 2002; it is plausible to postulate that releases during 1998 would have exposure potential for a cohort who was in utero in 1997. If an effect was present, this would be reflected in the 2002 school district records—the age (5 years old) this cohort would be entering the system.

Please cite this article as: Palmer, R.F., et al., Proximity to point sources of environmental mercury release as a predictor of autism prevalence. Health & Place (2008), doi:10.1016/j.healthplace.2008.02.001

Results

Table 1 shows the descriptive statistics of the study variables. Note that there is considerable variation in each variable. Table 2 shows the Poisson regression coefficients and the corresponding Incident Risk Ratio (IRR) for the models exploring the linear and non-linear association between 1998 mercury release from industrial sources, distance, and 2002 autism rates. Model 1a shows that environmentally released mercury in 1998 is significantly associated with autism rates in 2002. We multiplied the coefficient by 1000 to reflect increases in autism rates per 1000 pounds. The coefficient yields an IRR of 1.026, indicating that for every 1000 pounds of release in 1998, there is a corresponding 2.6% increase in 2002 autism rates. In model 1b, the squared term for pounds was entered into the model. Note that the linear coefficient is no longer significant and the polynomial term is. This indicates that the association between industrial sources of mercury release is non-linear—e.g. for every 1000 pounds there is an associated 1.1% accelerated risk. Adding distance to the equation in model 1c shows that

Table 1
Descriptive statistics of study variables

	Mean or percent	Standard deviation	Range
Predictor variables			
Total number pounds of mercury per year for power plants	1225 lb	946	8–2516
Total number pounds of mercury per year for industrial facilities	1526 lb	1909	3–6685
Minimum distance to industrial facilities	39.7 miles	29.3	0.34–170.4
Minimum distance to power plants	71.7 miles	53.2	0.74–305.8
Relevant demographic covariates			
Value of taxable property	$265,148	$328,631	0–$3,481,369
Percent urban	4%	–	–
Percent suburban	15%	–	–
Percent White	61.5%	–	0–100%
Proportion autism 1997 (rate per 1000)	0.85	2.1	0–26.3
Outcome variable			
Proportion autism 2002 (rate per 1000)	2.0	3.2	0–39.5

Table 2
2002 Autism rates as a function of industrial release of mercury in 1998

Model 1: 2002 autism rates as function of 1998 pounds of mercury emission from industrial sources	Amount of Hg (per 1000 lb)	Amount of Hg (per 1000 lb)^2	Distance to industrial sources per 10 miles	1997 autism rates	District Wealth (per $100,000)	Urban vs. rural	Suburban vs. rural	Percent White
Model 1a								
Regression coefficient (standard error)	**.026 (.010)***	–	–	–	–	–	–	–
Incident Risk Ratio	**1.026**	–	–	–	–	–	–	–
Model 1b								
Regression coefficient (standard error)	−.007 (.014)^{ns}	**.018 (.006)****	–	–	–	–	–	–
Incident Risk Ratio	–	**1.018**	–	–	–	–	–	–
Model 1c								
Regression coefficient (standard error)	.021 (.015)^{ns}	**.02 (.006)****	**−.014 (.006)***	–	–	–	–	–
Incident Risk Ratio	–	**1.020**	**0.986**	–	–	–	–	–
Model 1d								
Regression coefficient (standard error)	.003 (.011)^{ns}	**.018 (.005)****	**−.02 (.008)***	**.16 (.01)*****	**.047 (.01)****	**.29 (.04)*****	**.33 (.04)*****	**.004 (.001)****
Incident Risk Ratio	–	**1.018**	**.980**	**1.170**	**1.048**	**1.33**	**1.39**	**1.004**

Note: Second column reflects the amount of mercury squared, the non-linear polynomial term.
ns: not significant
*$p<.05$.
**$p<.01$.
***$p<.001$.

Please cite this article as: Palmer, R.F., et al., Proximity to point sources of environmental mercury release as a predictor of autism prevalence. Health & Place (2008), doi:10.1016/j.healthplace.2008.02.001

Table 3
2002 Autism rates as a function of power plant release of mercury in 1998

Model 2: 2002 autism rates as function of 1998 pounds of mercury emission from power plant sources	Pounds of Hg per 1000	Non-linear term (Pounds of Hg per 1000)^2	Distance to industrial sources per 10 miles	1997 autism rates	District Wealth (per $100,000)	Urban vs. rural	Suburban vs. rural	Percent White
Model 2a								
Regression coefficient (standard error)	**.037 (.018)***	–	–	–	–	–	–	–
Incident Risk Ratio	**1.037**	–	–	–	–	–	–	–
Model 2b								
Regression coefficient (standard error)	**.044 (.020)***	.050(.030)^{ns}	–	–	–	–	–	–
Incident Risk Ratio	**1.044**	–	–	–	–	–	–	–
Model 2c								
Regression coefficient (standard error)	.017 (.022)^{ns}	–	**.011 (.040)***	–	–	–	–	–
Incident Risk Ratio	–	–	**.989**	–	–	–	–	–
Model 2d								
Regression coefficient (standard error)	.003 (.011) ^{ns}	–	**.014 (.045)***	**.161 (.01)*****	**.045 (.01)****	**.290 (.04)*****	**.330 (.04)*****	**.005 (.001)****
Incident Risk Ratio	–	–	**.986**	**1.170**	**1.056**	**1.33**	**1.39**	**1.005**

Note: Second column reflects the amount of mercury squared, the non-linear polynomial term.
ns: not significant
* $p<.05$.
** $p<.01$.
*** $p<.001$.

for every 10 miles away from the source there is a decreased autism Incident Risk of 1.4%. Adding non-linear terms for distance (distance squared and the square root of distance) (not depicted) was not significant and therefore not utilized in other models. Model 1d is the fully adjusted model depicting that the positive non-linear term for pounds, and the inverse association for distance, remain independently associated with 2002 autism rates after adjustment for 1997 autism rates, urbanicity, racial composition, and district wealth. Urbanicity and 1997 autism rates demonstrate to be the strongest predictors of 2002 autism rates in the final model.

Table 3 shows the Poisson regression coefficients and the corresponding IRR for the models exploring the linear and non-linear association between 1998 mercury release from power plant sources, distance to these sources, and 2002 autism rates.

Model 2a shows that environmentally released mercury from power plants in 1998 is significantly associated with autism rates in 2002. For every 1000 pounds of release there is a corresponding 3.7% increase in autism rates. In model 2b, the squared term for pounds was entered into the model and was not significant and therefore, not used in the subsequent models. Adding distance to the equation in model 2c shows that for every 10 miles away from the source, there is a significant 1% decrease in the autism Incident Risk. A 20-mile distance would yield a 2.2% decreased risk. Adding non-linear distance terms (distance squared and the square root of distance) (not depicted) was not significant and therefore not utilized in the next model. Most importantly however, in model 2c, the coefficient for pounds is no longer significant. This suggests that the direct effect between pounds of release in 1998 and 2002 autism rates are fully explained by distance to the source of release. The fully adjusted model 2d shows that this effect remains independent after adjustment for the covariates.

Discussion

These results build upon two prior studies demonstrating an association between environmental mercury release and autism rates (Palmer et al., 2006; Windham et al., 2006). The current study shows that environmental mercury in 1998 is associated with autism rates in 2002 after adjusting for other relevant sociodemographic covariates including autism rates in 1997. This is consistent with the prior reports. The novel findings in this study are that distance to the sources of mercury release was independently related to autism rates. In the separate analysis of power plant emissions, distance to the source fully explained the association between total pounds of mercury release and autism rates.

We also found that the association between releases from industrial rather than power plant sources was non-linear—e.g. increases in pounds from industrial sites were associated with an accelerated risk function. This difference in the shapes of the exposure-response curve for industrial

Please cite this article as: Palmer, R.F., et al., Proximity to point sources of environmental mercury release as a predictor of autism prevalence. Health & Place (2008), doi:10.1016/j.healthplace.2008.02.001

release (exponential increase) versus release from power plants (linear) might be explained by the fact that pollution from industrial sources are relatively more localized and not as far spreading as pollution from power plants. It is reasonable to suspect that greater local release could cause exponential effects as compared to more widely distributed releases.

On the other hand, the non-linear functions for distance were not significantly related to the outcome. It is plausible to suspect that exposure mediated by distance from the source depends more on other factors such as characteristics of the physical environment and predominant wind or rain patterns rather than simply distance alone. Exposure from power plants can potentially span thousands of miles and modeling the kinds of factors that affect exposure over time would require data that are not readily available. Notwithstanding, the results demonstrate an overall inverse association between distance to the source of release and subsequent autism rates. While these effects are relatively small, they are significant and demonstrate potential public health risks.

Although a major limitation to this study is that we cannot verify exposure at the individual level, a host of other plant, animal and human studies have demonstrated that distance to sources of environmental mercury exposure are related to increased body burdens of mercury (Ordonez et al., 2003; Fernandez et al., 2000; Hardaway et al., 2002; Navarro et al., 1993; Kalac et al., 1991; Moore and Sutherland, 1981). However, the effects of duration and dose amounts of environmental exposures are not currently known—and we do not know that body burden of mercury is in fact related to the potential exposure measures used in these analyses.

Mercury is a known immune modulator (Moszczynski, 1997). These effects include the production of autoantibodies to myelin basic protein (El-Fawal et al., 1999) and effects on the ratio of Th1/Th2 immunity factors (Kroemer et al., 1996). This is consistent with the literature demonstrating similar types of altered immune function in autistic children (Singh et al., 1997; Singh and Rivas, 2004; Krause et al., 2002; Cohly and Panja, 2005; Vojdani et al., 2003). However, unlike the specific vector known about exposure through fish consumption, very little is known about exposure routes from seemingly randomly distributed ambient exposures in the environment—particularly in air.

Even if ambient air, ground exposure routes, and low-level toxic thresholds can be identified by researchers, differential genetic susceptibilities in the ability to metabolize heavy metals and other pollutants would still need to be considered in future research (Herbert et al., 2006). While inconclusive to date, the existing studies warrant the need for further investigation on environmental mercury pollution and the developmental health of children.

There are some important limitations to this manuscript that should be addressed. First, these data do not reflect the true community prevalence rates of autism, largely because children who are not of school age are not counted in the TEA data system. This is reflected in the $\frac{1}{500}$ autism rates for 2002 present in Table 1—which are lower than the current CDC reports of $\frac{1}{150}$ (CDC, 2007).

Further, individual risk cannot be inferred from population-based ecological studies such as this. Further, conclusions about exposure are limited, because distance was not calculated from individual homes to the pollution source, but from school district centroids of varying sizes. Rural school districts are usually larger in size than urban school districts and are one good reason to include urbanicty as covariates in these models.

This study should be viewed as hypothesis generating—a first step in examining the potential role of environmental mercury and childhood developmental disorders. Nothing is known about specific exposure routes, dosage, timing, and individual susceptibility. We suspect that persistent low-dose exposures to various environmental toxicants, including mercury, that occur during critical windows of neural development among genetically susceptible children (with a diminished capacity for metabolizing accumulated toxicants) may increase the risk for developmental disorders such as autism. Successfully identifying the specific combination of environmental exposures and genetic susceptibilities can inform the development of targeted prevention intervention strategies.

References

Amin-Zaki, L., Elhassani, S., Majeed, M.A., et al., 1988. Studies of infants postnatally exposed to methylmercury. Journal of Pediatrics 41, 475–482.

Agency for Toxic Substances and Disease Registry (ATSDR), 2001. CERCLA Priority List of Hazardous Substances. US Department of Health and Human Services, Public Health Service, Atlanta, GA ⟨http://www.atsdr.cdc.gov/cercla/⟩ (accessed 10/07).

Bernard, S., Enayati, A., Roger, H., Binstock, T., Redwood, L., 2002. The role of mercury in the pathogenesis of autism. Molecular Psychiatry 7, S42–S43.

Bradstreet, J., Geier, D., Kartzinel, J., Adams, J., Geier, M., 2003. A case–control study of mercury burden in children with autistic spectrum disorders. Journal of American Physicians and Surgeons 8 (3), 76–79.

Centers for Disease Control and Prevention, 2007. Prevalence of Autism Spectrum Disorders—Autism and Developmental Disabilities Monitoring Network, Six Sites, United States, 2000, Surveillance Summaries, MMWR 56 (No. SS-1).

Cohly, H.H., Panja, A., 2005. Immunological findings in autism. International Review of Neurobiology 71, 317–341.

Ebinghaus, R., Kock, H., Schmolke, S., 2001. Measurements of atmospheric mercury with high time resolution: recent applications in environmental research and monitoring. Fresenius Journal of Analytical Chemistry 371, 806–815.

Eisenmajer, R., Prior, M., Leekam, S., Wing, L., Gould, J., Welham, M., 1996. Comparison of clinical symptoms in autism and Asperger's disorder. Journal of the American Academy of Child and Adolescent Psychiatry 35 (11), 1523–1531.

El-Fawal, HA., Waterman, S.J., De Feo, A., Shamy, M.Y., 1999. Neuroimmunotoxicology: humoral assessment of neurotoxicity and autoimmune mechanisms. Environmental Health Perspectives 107 (Suppl 5), 767–775.

Environmental Protection Agency, 1997. Mercury study report to Congress. Publication number: EPA 452/R97-003.

Please cite this article as: Palmer, R.F., et al., Proximity to point sources of environmental mercury release as a predictor of autism prevalence. Health & Place (2008), doi:10.1016/j.healthplace.2008.02.001

Fernandez, J.A., Aboal, J.R., Carballeira, A., 2000. Use of native and transplanted mosses as complementary techniques for biomonitoring mercury around an industrial facility. Science of the Total Environment 256 (2–3), 151–161.

Freed, G.L., Andreae, M.C., Cowan, A.E., Katz, S.L., 2002. The process of public policy formulation: the case of thimerosal in vaccines. Pediatrics 109, 1153–1159.

Geier, D., Geier, M.A., 2006. Prospective Assessment of porphyrins in Autistic disorders: a potential marker for heavy metal exposure. Neurotoxicity Research 10 (1), 57–64.

Grandjean, P., Jørgensen, P.J., Weihe, P., 1994. Human milk as a source of methylmercury exposure in infants. Environmental Health Perspectives 102, 74–77.

Grandjean, P., Weihe, P., White, R.F., 1995. Milestone development in infants exposed to methylmercury from human milk. Neurotoxicology 16, 27–33.

Hardaway, C., Gauthreaux, K., Sneddon, J., Beck, J.N., 2002. Atomic absorption spectrometric determination of chromium, copper, lead, mercury, and zinc in sediments collected in Bayou d'Inde, southwestern Louisiana. Journal of AOAC International 85 (1), 225–232.

Hill, A., Bolte, S., Petrova, G., Beltcheva, D., Tacheva, S., Poustka, F., 2001. Stability and interpersonal agreement of the interview-based diagnosis of autism. Psychopathology 34 (4), 187–191.

Holmes, A.S., Blaxill, M.F., Haley, B.E., 2003. Reduced levels of mercury in first baby haircuts of autistic children. International Journal of Toxicology 22, 277–285.

Herbert, M.R., Russo, J.P., Yang, S., Roohi, J., Blaxill, M., Kahler, S., Cremer, L., Hatchwell, E., 2006. Autism and Environmental Genomics. Neurotoxicology 27, 671–684.

Kalac, P., Burda, J., Staskova, I., 1991. Concentrations of lead, cadmium, mercury and copper in mushrooms in the vicinity of a lead smelter. Science of the Total Environment 105, 109–119.

Krause, I., He, X.S., Gershwin, M.E., Shoenfeld, Y., 2002. Brief report: immune factors in autism: a critical review. Journal of Autism and Developmental Disorders 32 (4), 337–345.

Kroemer, G., Hirsch, F., Gonzalez-Garcia, A., Martinez, C., 1996. Differential involvement of Th1 and Th2 cytokines in autoimmune diseases. Autoimmunity 24 (1), 25–33.

Kurttio, P., Pekkanen, J., Alfthan, G., Paunio, M., Jaakkola, J., Heinonen, O., 1998. Increased mercury exposure in inhabitants living in the vicinity of a hazardous waste incinerator: a 10-year follow-up. Archives of Environmental Health 53 (2), 129–137.

Landrigan, P.J., Garg, A., 2002. Chronic effects of toxic environmental exposures on children's health. Journal of Toxicology—Clinical Toxicology 40 (4), 449–456.

MacGregor, A., 1975. Analysis of control methods: mercury and cadmium pollution. Environmental Health Perspectives 12, 137–148.

Mahaffey, K.R., 1999. Methylmercury: a new look at the risks. Public Health Reports 114 (5), 396–399, (402–413).

Mahoney, W., Szatmari, P., MacLean, J., Bryson, S., Bartolucci, G., Walter, S., 1998. Reliability and accuracy of differentiating pervasive developmental disorder subtypes. Journal of the American Academy of Child and Adolescent Psychiatry 37 (3), 278–285.

Moore, J., Sutherland, D., 1981. Distribution of heavy metals and radionuclides in sediments, water, and fish in an area of great bear lake contaminated with mine wastes. Archives of Environmental Contamination and Toxicology 10 (3), 329–338.

Moszczynski, P., 1997. Mercury compounds and the immune system: a review. International Journal of Occupational Medicine and Environmental Health 10 (3), 247–258.

Nataf, R., Skorupka, C., Amet, L., Lam, A., Springbett, A., Lathe, R., 2006. Porphyinuria in childhood autistic disorder: implications for environmental toxicity. Toxicology and Applied Pharmcology 214, 99–108.

National Academy of Sciences, 2000. Toxicological Effects of Methylmercury. National Academy Press, Washington, DC.

Navarro, M., Lopez, H., Sanchez, M., Lopez, M.C., 1993. The effect of industrial pollution on mercury levels in water, soil, and sludge in the coastal area of Motril, southeast Spain. Archives of Environmental Contamination and Toxicology 24 (1), 11–15.

Ordonez, A., Loredo, J., De Miguel, E., Charlesworth, S., 2003. Distribution of heavy metals in the street dusts and soils of an industrial city in northern Spain. Archives of Environmental Contamination and Toxicology 44 (2), 160–170.

Oskarsson, A., Schutz, A., Skerfving, S., Hallen, I., Ohlin, B., Lagerkvist, B., 1996. Total and inorganic mercury in breast milk and blood in relation to fish consumption and amalgam fillings in lactating women. Archives of Environmental Health 51 (3), 234–241.

Palmer, R., Blanchard, S., Jaen, C., Mandell, S., 2005. The association between school district resources and identification of children with autistic disorder. American Journal of Public Health 95 (1), 125–130.

Palmer, R.F., Blanchard, S., Stein, Z., Mandell, D., Miller, C., 2006. Environmental mercury release, special education rates, and Autism disorder: an ecological study of Texas. Health and Place 12, 203–209.

Ramirez, G., Pagulayan, O., Akagi, H., et al., 2003. Tagum study II: follow-up study at two years of age after prenatal exposure to mercury. Pediatrics 111 (3), e289–e295.

Rasbash, J., Browne, W., Goldstein, H., Yang, M., Plewis, I., Healy, M., Woodhouse, G., Draper, D., 1999. A User's Guide to MLwiN. Institute of Education, London.

Rice, D., Barone, S., 2000. Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. Environmental Health Perspectives 108 (Suppl 3), 511–533.

Rowland, I.R., Robinson, R.D., Doherty, R.A., et al., 1983. Are developmental changes in methylmercury metabolism and excretion mediated by the intestinal microflora? In: Reproductive and Developmental Toxicity of Metals. Plenum Press, New York, pp. 745–758.

Schechter, R., Grether, J., 2008. Continuing increases in Autism reported to California's developmental services system. Archives of General Psychiatry 65 (1), 19–24.

Schuster, P.F., Krabbenhoft, D.P., Naftz, D.L., Cecil, L.D., Olson, M.L., Dewild, J.F., Susong, D.D., Green, J.R., Abbott, M.L., 2002. Atmospheric mercury deposition during the last 270 years: a glacial ice core record of natural and anthropogenic sources. Environmental Science and Technology 36 (11), 2303–2310.

Singh, V.K., Rivas, W.H., 2004. Prevalence of serum antibodies to caudate nucleus in autistic children. Neuroscience Letters 355 (1–2), 53–56.

Singh, V.K., Warren, R., Averett, R., Ghaziuddin, M., 1997. Circulating autoantibodies to neuronal and glial filament proteins in autism. Pediatric Neurology 17 (1), 88–90.

Sundberg, J., Oskarsson, A., Bergman, K., 1991a. Milk transfer of inorganic mercury to suckling rats. Interaction with selenite. Biological Trace Element Research 28, 27–38.

Sundberg, J., Oskarsson, A., Albanus, L., 1991b. Methylmercury exposure during lactation: milk concentration and tissue uptake of mercury in the neonatal rat. Bulletin of Environmental Contamination and Toxicology 46, 255–262.

Thomas, D.J., Smith, J.C., 1979. Distribution and excretion of mercuric chloride in neonatal rats. Toxicology and Applied Pharmacology 48, 43–47.

United States Environmental Protection Agency Toxics Release Inventory, 2006. ⟨http://www.epa.gov/tri⟩ Accessed 10/07. USEPA-TRI.

Vojdani, A., Pangborn, J.B., Vojdani, E., Cooper, E.L., 2003. Infections, toxic chemicals and dietary peptides binding to lymphocyte receptors and tissue enzymes are major instigators of autoimmunity in autism. International Journal of Immunopathology and Pharmacology 16 (3), 189–199.

Wang, D., Shi, X., Wei, S., 2003. Accumulation and transformation of atmospheric mercury in soil. Science of the Total Environment 304 (1–3), 209–214.

Windham, G.C., Zhang, L., Gunier, R., Croen, L.A., Grether, J.K., 2006. Autism spectrum disorders in relation to distribution of hazardous air pollutants in the San Francisco Bay area. Environmental Health Perspectives 114 (9), 1438–1444.

Yeargin-Allsopp, M., Rice, C., Karapurkar, T., Doernberg, N., Boyle, C., Murphy, C., 2003. Prevalence of autism in a US metropolitan area. Journal of the American Medical Association 289, 49–55.

Please cite this article as: Palmer, R.F., et al., Proximity to point sources of environmental mercury release as a predictor of autism prevalence. Health & Place (2008), doi:10.1016/j.healthplace.2008.02.001

EXHIBIT 5

ELSEVIER

Health & Place ▮ (▮▮▮▮) ▮▮▮–▮▮▮

HEALTH & PLACE

www.elsevier.com/locate/healthplace

Environmental mercury release, special education rates, and autism disorder: an ecological study of Texas

Raymond F. Palmer[a,*], Steven Blanchard[b], Zachary Stein[a], David Mandell[c], Claudia Miller[a]

[a]*University of Texas Health Science Center, San Antonio Department of Family and Community Medicine, 7703 Floyd Curl Drive, San Antonio, Texas 78229-3900, USA*

[b]*Department of Sociology, Our Lady of the Lake University, San Antonio, Texas, USA*

[c]*University of Pennsylvania Center for Mental Health Policy and Services Research, USA*

Accepted 1 November 2004

Abstract

The association between environmentally released mercury, special education and autism rates in Texas was investigated using data from the Texas Education Department and the United States Environmental Protection Agency. A Poisson regression analysis adjusted for school district population size, economic and demographic factors was used. There was a significant increase in the rates of special education students and autism rates associated with increases in environmentally released mercury. On average, for each 1000 lb of environmentally released mercury, there was a 43% increase in the rate of special education services and a 61% increase in the rate of autism. The association between environmentally released mercury and special education rates were fully mediated by increased autism rates. This ecological study suggests the need for further research regarding the association between environmentally released mercury and developmental disorders such as autism. These results have implications for policy planning and cost analysis.

Keywords: Mercury; Special education; Autism; Environmental toxins; Ecological

Introduction

Exposure to a variety of environmental neurotoxicants is known to affect normal child development, resulting in a spectrum of adverse outcomes, ranging from severe mental retardation and developmental disability to more subtle changes in functioning, depending in part on the timing and dose of the chemical agent (Landrigan and Garg, 2002; Mendola et al., 2002; Rice and Barone, 2000).

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) section 104 (i), as amended by the Superfund Amendments and Reauthorization Act (SARA), requires the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency (EPA) to prepare a list, in order of priority, of substances that are most commonly found at waste facilities on the National Priorities List (NPL) and which are determined to pose the most significant potential threat to human health due to their known or suspected toxicity and potential for human exposure. Accordingly, mercury is listed as the third-most frequently found (arsenic and lead are

*Corresponding author. Tel.: +210 358 3883.
E-mail address: palmerr@uthscsa.edu (R.F. Palmer).

1353-8292/$ - see front matter © 2005 Published by Elsevier Ltd.
doi:10.1016/j.healthplace.2004.11.005

first and second) toxic substance in the United States (ATSDR, 2001).

Symptoms of nervous system disruption associated with chronic exposure to mercury has been known since the 19th century, when mercury was widely used in the felt industry which led to the expression of "hatter's disease" (Hu, 1998). Further epidemiological evidence of the neurotoxicity of mercury dates back to the 1950s, when it was ascertained that thousands of people in Minamata and Niigata Japan suffered various neurological impairments caused by consumption of mercury contaminated fish (Harada, 1978). However, the neurotoxicity of low-level mercury exposure has only recently been documented (NAS, 2000; EPA, 1997) and recent reports implicate mercury in the etiology of various developmental and learning disabilities (Ramirez et al., 2003; Grandjean et al., 2003) including autism (Bernard et al., 2001, 2002).

Recent evidence for mercury toxicity relevant to the biology of autism is compelling (Palomo et al., 2003; Aschner and Walker, 2002; Bernard et al., 2002; Vojdani et al., 2003) and Bradstreet et al. (2003) report that levels of urinary mercury after a 3-day treatment with an oral chelating agent, meso-2,3-dimercaptosuccinic acid (DMSA), in children with autistic spectrum disorders were three times those in a matched normal control sample.

Environmentally released mercury is a major source of mercury exposure. Mercury is released into the environment largely from fossil fuel (mainly coal) combustion by electrical utilities and from municipal and medical waste incinerators. This inorganic mercury becomes airborne and may be carried for miles before being deposited on soil or water. This inorganic form of mercury is then converted to a toxic form (methylmercury) by chemical reactions or by bacteria, which is absorbed by aquatic microorganisms that are eaten by fish, and in this manner accumulates up the aquatic food chain. Humans are primarily exposed through fish consumption (Myers et al., 2000) and transmission from mothers to infants is well documented in animal models (Newland et al., 1994) and human studies (Ramirez et al., 2000; Grandjean et al., 1995). Results from several studies show that maternal mercury exposure during pregnancy is associated with neuropsychological deficits in children and that this association is most evident in women with stable exposures throughout pregnancy (Ramirez et al., 2003; Grandjean et al., 2003).

Other than accidental poisoning at the population level, where developmental disabilities have been reported as the result of large mercury spills (Racz and Vandewater, 1982), there have been no published studies examining the risk of disability associated with mercury released into the environment within the current legal limits. The available information regarding exposure to toxic agents associated with developmental disorders is suggestive but inconclusive (Ostrowski et al., 2003). In a prior study, we report evidence for an association between environmentally released mercury and various developmental disorders, including autism, at the state level ($n = 50$) (unpublished manuscript). We considered the positive association between developmental disabilities and environmentally released mercury in that investigation as preliminary due to the relatively small number of large geological regions. In this study, we investigate the association between environmentally released mercury pollution and autism rates at the county ($n = 254$) and school district level ($n = 1184$) in Texas. The advantage of using county level data in this study allows an investigation using greater numbers of smaller geographic units in the analysis—this can potentially increase our power to detect an effect if in fact it present. Since Texas ranks 4th among states with the highest reported mercury releases (next to California, Oregon, and West Virginia) (USEPA-TRI, 2004), analysis of data from this state can be useful for further investigation of the association between environmental mercury release and developmental disorders. In this study, we investigate the association between total special education rates, autism, and environmental mercury release.

Methods

Data source and sample data regarding environmentally released mercury for each county were obtained from the United State Environmental Protection Agency Toxics Release Inventory (TRI) (USEPA-TRI, 2004). TRI collects information about chemical releases and waste management reported by major industrial facilities in the US. The TRI database was established by Section 313 of the Emergency Planning and Community Right-To-Know Act of 1986 (EPCRA). Under EPCRA, industrial facilities in specific sectors are required to report their environmental releases and waste management practices annually to the EPA. Facilities covered by this act must disclose their releases to air, water, and land of approximately 650 toxic chemicals, as well as the quantities of chemicals they recycle, treat, burn, or otherwise dispose of on-site and off-site. The current analysis uses reports of pollution that industrial facilities provided to TRI for the calendar year 2001. The total number of pounds of environmentally released mercury was obtained for each county.

Administrative data from the Texas Education Agency (TEA) from school years 2000–2001 were analyzed. Data and data description are available at the TEA website at http://198.214.99.202. In compliance with the Texas Education Code, the Public Education Information Management System (PEIMS) contains

data necessary for the legislature and the TEA to perform their legally authorized functions in overseeing public education. The database consists of student demographic, personnel, financial, and organizational information. Autism counts per school district were obtained by special request from the TEA. Data were from 1184 school districts in 254 counties in Texas. These districts represented approximately 4 million children enrolled in grades K through 12.

Diagnosis of autistic disorder was abstracted from the school record for each year of the study period. Diagnoses were made by qualified special education psychologists employed by the TEA or from psychologists or medical doctors outside the TEA system. While diagnoses were not standardized, there is considerable evidence that diagnoses of autistic disorder are made with good reliability and specificity in the field (Eisenmajer et al., 1996; Hill et al., 2001, Mahoney et al., 1998).

District population wealth was calculated as a school district's total taxable property value in 2001 as determined by the Comptroller's Property Tax Division (CPTD), divided by the total number of students in the district in 2000–2001. Property value was determined by the CPTD as part of its annual study, which attempts to present uniformly appraised property valuations statewide. The CPTD value is calculated by applying ratios created from uniform independent appraisals to the district's assessed valuations.

Racial composition was accounted for by the proportion of European-American children enrolled in schools within each district.

Total number of students was calculated as all enrolled students as of October 28, 2000 in grades kindergarten through twelve, who attended at least 1 day of school for that school year. Statewide, 6975 students, or 0.2% of all students, were enrolled but did not attend school.

Proportion of economically disadvantaged students was calculated as the percentage of students who were eligible for free meals under the National School Lunch and Child Nutrition Program, reduced-price meals under the National School Lunch and Child Nutrition Program, or other public assistance.

Total number of students enrolled in special education was calculated as the number of students receiving special education in each district.

Urbanicity. Eight separate demographic district regions were utilized in the analysis: (1) *Major urban* districts are the districts with the greatest membership in counties with populations of 650,000 or more, and more than 35% of the students are identified as economically disadvantaged. (2) *Other central city*—The major school districts in other large, but not major, Texas cities. Other central city districts are the largest districts in counties with populations between 100,000 and 650,000 and are not contiguous to any major urban districts. (3) *Major suburban* districts are contiguous to major urban districts. If the suburban district is not contiguous, it must have a student population that is at least 15% of the size of the district designated as major urban. (4) *Other central city suburban*—Other school districts in and around the other large, but not major, Texas cities. They are contiguous to other central city districts. If the suburban district is not contiguous, it must have a student population that is at least 15% of the size of the district designated as central city. (5) *Independent town*—The largest school districts in counties with populations of 25,000–100,000. (6) *Non-metro: fast growing* school districts that are not in any of the above categories and that exhibit a 5-year growth rate of at least 20%. These districts must have at least 300 students in membership. (7) *Non-metro: stable* school districts that are not in any of the above categories, yet have a number of students in membership that exceeds the state median. (8) *Rural* school districts that do not meet the criteria for placement into any of the above categories. These districts either have a growth rate less than 20% and the number of students in membership is between 300 and the state median, or the number of students in membership is less than 300.

In the analysis, the first two categories above were combined to form an "urban" dummy variable, categories three and four were combined to form a "suburban" dummy variable and categories five through seven formed an "other" category, with rural districts as the reference group.

Statistical methods. Since the 1184 school districts were nested within 254 counties, we modeled the data using a multilevel Poisson regression model to adjust estimates due to a potential county level clustering effect—which can bias estimated standard errors downward, thus leading to type I errors if not properly addressed (Barcikowski, 1981).

A multilevel Poisson regression model allowing for over-dispersion of the dependent variable was used in which the total number of children with autism and the number of special education students (excluding autism) was modeled separately as a function of the total pounds of environmentally released mercury. The model was adjusted for percent of the population of European-American descent, district population wealth, percent economically disadvantaged and urbanicity. Rates were offset by the total number of children served in a school district. For the model predicting autism rates, special education counts were included as a covariate in a subsequent model. For the model predicting special education rates, autism counts were also included as a covariate in a separate model. All models were estimated using MLwiN software with a log link function specified (Goldstein et al., 1998). The analysis yields adjusted relative rate estimates as a function of pounds of environmentally released mercury.

Results

Table 1 shows the descriptive statistics of the study variables. The standard deviation and the maximum and minimum values indicate considerable variation for all study variables. Table 2 shows the results of the regression model where autism rates were modeled as a function of pounds of mercury and sociodemographic covariates (model 1), plus adjustment for the number of special education students (excluding autism) (model 2).

Model 1 shows that for each 1000 lb of environmentally released mercury, the rate of autism increases by 61%. A small but significant rate increase is noted for districts with higher wealth, and a small but significant inverse association is observed for percentage of European American and economically disadvantaged students. A large effect is observed for community type. The highest rate increase is observed when comparing urban to rural school districts—relative to rural districts there is a 473% higher rate of autism. There is a 255%

Table 1
Descriptive statistics for study variables ($n = 1184$ school districts in 254 counties)

	Mean	SD	Minimum	Maximum
Autism count total	5.11	21.39	0	416
Total special education population count	414.12	1205.21	0	21,900
Pounds of environmental mercury release	203.99	522.84	0	2059
Total student population	3382.30	10908.99	6	209,916
Percent economically disadvantaged	47.28	21.70	0	100
Percent European American	58.33	29.71	0	100
District wealth	$189,080	$262,290	0	$4,276,736
Community type				
% Urban	4.1	—	—	—
% Suburban	13.2	—	—	—
% Rural	34.9	—	—	—
% Other	47.8	—	—	—

Table 2
Poisson regression estimates predicting relative rate of autism prevalence

	Estimate (SE)	Relative rate	Lower 95% CI	Upper 95% CI
Model 1: Predicting autism prevalence rates as a function of mercury release with demographic covariate adjustments				
Mercury (per 1000 pounds)	0.479 (0.041)	1.614	1.487	1.752
Percent European American	−0.023 (.001)	0.977	0.975	0.979
District wealth (per 100,000 dollars)	0.060 (0.010)	1.062	1.041	1.083
Percent economically disadvantaged	−0.029 (0.001)	0.971	0.969	0.973
Urban versus rural	1.553 (0.109)	4.726	3.800	5.877
Suburban versus rural	0.935 (0.108)	2.547	2.052	3.161
Other versus rural	0.027 (0.112)	1.027	0.821	1.285
Model 2: Predicting autism prevalence rates as a function of mercury with demographic and special education count adjustment				
Mercury (per 1000 pounds)	0.160 (0.031)	1.174	1.103	1.249
Percent European American	−0.019 (0.001)	0.981	0.979	0.983
District wealth (per 100,000 dollars)	0.010 (0.010)	1.010	0.990	1.030
Percent economically disadvantaged	−0.034 (0.001)	0.967	0.965	0.969
Urban versus rural	0.953 (0.078)	2.593	2.219	3.031
Suburban versus rural	0.808 (0.074)	2.243	1.935	2.601
Other versus rural	−0.356 (0.087)	0.700	0.589	0.834
Special education count (per 1000)	0.172 (0.005)	1.188	1.176	1.200

higher rate of autism in suburban relative to rural districts.

In model 2, after adjustment for the number of special education students, mercury remained a significant predictor of autism rates, indicating a 17% increase in autism rates for every 1000 lb of mercury released in the environment. The number of special education students was a significant predictor of autism rates as well. Wealth was no longer a significant predictor and the other covariates showed decreases relative to model 1, but remained significant.

Table 3 shows the regression estimates where special education rates (excluding autism counts) were modeled as a function of pounds of mercury and sociodemographic covariates (model 3), plus adjustment for the number of autistic students (model 4).

Model 3 shows that each 1000 lb of reported mercury release is associated with a 43% increase in the rate of special education students. Small but significant increases were associated with the percentage of European Americans, economically disadvantaged and district wealth. Community type was strongly associated with special education rates. All community-type categories show a much higher percentage of special education students relative to rural communities.

In model 4, after adjusting for total autism counts, the association between pounds of mercury and special education rates was no longer statistically significant—with the other covariates in the model remaining significant. This indicates that increased rates in autism account for the association between environmentally released mercury and the rate of special education students.

Discussion

To the best of our knowledge, this is one of the first investigations to report an ecological association between developmental disorders and environmentally released mercury.

The results of this study demonstrate that school district autism and special education rates are significantly associated with environmentally released mercury. This association was independent of the number of children served in the educational system for that district, district wealth, ethnic make-up, and community type. Further, these results indicate that the association between mercury release and school district special education rates was completely accounted for by increased rates of autism. This indicates that, in Texas, the increase in special education rates attributable to environmental mercury can be explained by increases in autism. The results of this study are consistent with our prior nation-wide study where an association between various developmental disabilities and environmentally released mercury was observed at the state level

Table 3
Poisson regression estimates predicting relative rate of special education prevalence

	Estimate (SE)	Relative rate	Lower 95% CI	Upper 95% CI
Model 3: Predicting special education prevalence rates as a function of mercury with demographic adjustments				
Mercury (per 1000 pounds)	0.360 (0.030)	1.433	1.350	1.522
Percent white	0.004 (0.001)	1.004	1.002	1.006
District wealth (per $100,000)	0.050 (0.010)	1.051	1.030	1.073
Percent economically disadvantaged	0.012 (0.001)	1.012	1.010	1.014
Urban versus rural	2.741 (0.104)	15.502	12.591	19.087
Suburban versus rural	2.110 (0.103)	8.248	6.713	10.135
Other versus rural	1.550 (0.110)	4.711	3.781	5.871
Model 4 Predicting special education prevalence rates as a function of mercury with demographic and autism count adjustments				
Mercury (per 1000 pounds)	−0.062 (0.032)	0.940	0.882	1.002
Percent white	0.008 (0.001)	1.008	1.006	1.010
District wealth (per $100,000)	0.030 (0.010)	1.030	1.010	1.051
Percent economically disadvantaged	0.014 (0.001)	1.014	1.012	1.016
Urban versus rural	2.240 (0.068)	9.393	8.199	10.762
Suburban versus rural	1.902 (0.066)	6.699	5.871	7.645
Other versus rural	1.174 (0.073)	3.235	2.795	3.743
Autism count (per 100)	0.689 (0.022)	1.992	1.906	2.081

(unpublished manuscript). However, the results of this report should be interpreted with caution for a number of reasons.

First, this is an ecological study that precludes interpretation at the individual level. We have used aggregate units in this analysis to investigate differential rates of autism as a function of pounds of mercury at the county level. While we properly addressed the potentially biasing effects of clustering (school districts nested within counties) by utilizing appropriate analytic methods (e.g. multilevel-analysis), individual data are required to make a better case for the observed associations and their interpretations. Nevertheless, ecological studies of this type are often an important first step in identifying subsequent areas of investigation.

Second, a causal association between environmentally released mercury and developmental disorders cannot be determined from this cross-sectional data. Data availability permitting, future studies could investigate this association by using longitudinal data where changes in mercury levels over time may be used as a predictor of the rate of change in developmental disorders over time.

Third, we should consider that school-based administrative autism data, such as these, are only a proxy for true community prevalence. However, these autism rates are most likely biased downward. For example, Yeargin-Allsopp et al. (2003) found that, in one metropolitan area, 18% of children who qualified for a diagnosis of autism according to their study criteria were receiving special education services but had not been categorized as having autism. The critical unknown issue is whether identification of children in the special education system is systematically biased in the same direction as reporting of environmental mercury release. For example, counties in which administrations are more aggressive regarding penalties for underreporting toxic release may also have educational policies that result in a greater number of children identified for special education services. Despite the limitations of these administrative data, as demonstrated, these data can be a useful component to preliminary epidemiological studies (Dales et al., 2001). By demonstrating an association between environmentally released mercury and developmental disorders, the results of this study provide a necessary first step in identifying plausible contributing factors of risk for developmental disabilities.

This line of research has implications for toxic substance regulation and prevention policies. The effects of differing state policies regarding toxic release of mercury on the incidence of developmental disorders should be investigated. For example, policies that have successfully limited exposures to lead have had direct effects on morbidity and have demonstrated reductions in health care costs related to lead exposure (Sargent et al., 1999, Galke et al., 2001; Brown, 2002). However, while federal efforts toward reducing mercury exposure through policy have been successful to some extent by signing bills into law, proportionally few have been enacted (Mercury Policy Project (MMP), 2004). Despite existing policy recommendations, debate concerning acceptable levels of safety still remains (Dourson et al., 2001; Kaiser, 2000), thus, limiting progress toward evaluating policies related to reducing exposure to mercury.

Conclusions

What is currently known about the low-level toxicity of mercury from behavioral toxicology and behavioral teratology studies are convincing enough to warrant further study. This study is among the first to demonstrate an association between environmentally released mercury at the county level and the rate of developmental disability. Given the limitations of this ecological association, future studies should investigate this association using other methodologies and samples. This line of research has important implications for public health policy and supports prior recommendations for reducing environmentally released mercury (Needleman, 1995; Landrigan et al., 1994).

References

Agency for Toxic Substances and Disease Registry (ATSDR), 2001. CERCLA Priority List of Hazardous Substances. US Department of Health and Human Services, Public Health Service, Atlanta, GA. www.atsdr.cdc.gov/clist.html.

Aschner, M., Walker, S.J., 2002. The neuropathogenesis of mercury toxicity. Molecular Psychiatry 7 (Suppl. 2), S40–S41.

Barcikowski, R., 1981. Statistical power with group mean as the unit of analysis. Journal of Educational Statistics 6, 267–285.

Bernard, S., Enayati, A., Redwood, L., Roger, H., Binstock, T., 2001. Autism: a novel form of mercury poisoning. Medical Hypotheses 56, 462–471.

Bernard, S., Enayati, A., Roger, H., Binstock, T., Redwood, L., 2002. The role of mercury in the pathogenesis of autism. Molecular Psychiatry 7, S42–S43.

Bradstreet, J., Geier, D., Kartzinel, J., Adams, J., Geier, M., 2003. A case-control study of mercury burden in children with autistic spectrum disorders. Journal of American Physicians and Surgeons 8 (3), 76–79.

Brown, M.J., 2002. Costs and benefits of enforcing housing policies to prevent childhood lead poisoning. Medical Decision Making 22 (6), 482–492.

Dales, L., Hammer, S., Smith, N., 2001. Time trends in autism and in MMR immunization coverage in California. Journal of the American Medical Association 285 (9), 1183–1185.

Dourson, M.L., Wullenweber, A.E., Poirier, K.A., 2001. Uncertainties in the reference dose for methylmercury. Neurotoxicology 22 (5), 677–689.

Eisenmajer, R., Prior, M., Leekam, S., Wing, L., Gould, J., Welham, M., 1996. Comparison of clinical symptoms in autism and Asperger's disorder. Journal of the American Academy of Child & Adolescent Psychiatry 35 (11), 1523–1531.

Environmental Protection Agency, 1997. Mercury Study Report to congress, vol 1. Available at: http://www.epa.gov/ttnatw01/112nmerc/volume1.pdf. Accessed February 22, 2004.

Galke, W., Clark, S., Wilson, J., et al., 2001. Evaluation of the HUD lead hazard control grant program: early overall findings. Environmental Research 86 (2), 149–156.

Goldstein, H., Rasbash, J., Plewis, I., Draper, D., Browne, W., Yang, M., Woodhouse, G., Healy, M.A., 1998. User's guide to MLwiN, Version 1.0, January. Institute of Education. ISBN 085473 547X.

Grandjean, P., Weihe, P., White, R.F., 1995. Milestone development in infants exposed to methylmercury from human milk. Neurotoxicology 16, 27–33.

Grandjean, P., White, R.F., Weihe, P., Jorgensen, P.J., 2003. Neurotoxic risk caused by stable and variable exposure to methylmercury from seafood. Ambulatory Pediatrics 3 (1), 18–23.

Harada, M., 1978. Congenital Minamata disease: intrauterine methylmercury poisoning. Teratology 18, 285–288.

Hill, A., Bolte, S., Petrova, G., Beltcheva, D., Tacheva, S., Poustka, F., 2001. Stability and interpersonal agreement of the interview-based diagnosis of autism. Psychopathology 34 (4), 187–191.

Hu, H., 1998. Heavy metal poisoning. In: Fauci, A.S., Braunwald, E., Isselbacher, K.J., Wilson, J.D., Martin, J.B., Kasper, D.L., Hauser, S.L., Longo, D.L. (Eds.), Harrison's Principles of Internal Medicine, 14th ed. McGraw-Hill, New York, pp. 2564–2569 (Chapter 397).

Kaiser, J., 2000. Mercury report backs strict rules. Science 289, 371–372.

Landrigan, P.J., Garg, A., 2002. Chronic effects of toxic environmental exposures on children's health. Journal of Toxicology—Clinical Toxicology 40 (4), 449–456.

Landrigan, P.J., Graham, D.G., Thomas, R.D., 1994. Environmental neurotoxic illness: research for prevention. Environmental Health Perspectives 102 (Suppl. 2), 117–120.

Mahoney, W., Szatmari, P., MacLean, J., Bryson, S., Bartolucci, G., Walter, S., 1998. Reliability and accuracy of differentiating pervasive developmental disorder subtypes. Journal of the American Academy of Child & Adolescent Psychiatry 37 (3), 278–285.

Mendola, P., Selevan, S.G., Gutter, S., Rice, D., 2002. Environmental factors associated with a spectrum of neurodevelopmental deficits. Mental Retardation Developmental Disabilities Research Reviews 8 (3), 188–197.

Mercury Policy Project (MMP), 2004. Web site. Available at http://www.mercurypolicy.org. Accessed March 1.

Myers, G.J., Davidson, P.W., Cox, C., Shamlaye, C., Cernichiari, E., Clarkson, T.W., 2000. Twenty-seven years studying the human neurotoxicity of methylmercury exposure. Environmental Research 83 (3), 275–285.

National Academy of Sciences, 2000. Toxicological Effects of Methylmercury. National Academy Press, Washington, DC.

Needleman, H.L., 1995. Behavioral toxicology. Environmental Health Perspectives 103 (Suppl. 6), 77–79.

Newland, M.C., Yezhou, S., Logdberg, B., Berlin, M., 1994. Prolonged behavioral effects of in utero exposure to lead or methyl mercury: reduced sensitivity to changes in reinforcement contingencies during behavioral transitions and in steady state. Toxicology and Applied Pharmacology 126, 6–15.

Ostrowski, S., Wilbur, S., Chou, C., Pohl, H., Stevens, Y., Allred, P., Roney, N., Fay, M., Tylenda, C., 2003. Agency for Toxic Substances and Disease Registry's 1997 priority list of hazardous substances. Latent effects—carcinogenesis, neurotoxicology, and developmental deficits in humans and animals. Toxicology & Industrial Health 15 (7), 602–644.

Palomo, T., Beninger, R.J., Kostrzewa, R.M., Archer, T., 2003. Brain sites of movement disorder: genetic and environmental agents in neurodevelopmental perturbations. Neurotoxological Research 5 (1–2), 1–26.

Racz, W., Vandewater, L., 1982. Perspectives on the central nervous system toxicity of methylmercury. Canadian Journal of Physiology and Pharmacology 60, 1037–1045.

Ramirez, G., Vince Cruz, C., Pagulayan, O., Ostrea, E., Dalisay, C., 2000. The Tagum Study I: analysis and clinical correlates of mercury in maternal and cord blood, breast milk, meconium, and infants' hair. Pediatrics 106 (4), 774–781.

Ramirez, G., Pagulayan, O., Akagi, H., et al., 2003. Tagum study II: follow-up study at two years of age after prenatal exposure to mercury. Pediatrics 111 (3), e289–e295.

Rice, D., Barone, S., 2000. Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. Environmental Health Perspectives 108 (Suppl 3), 511–533.

Sargent, J.D., Dalton, M., Demidenko, E., Simon, P., Klein, R.Z., 1999. The association between state housing policy and lead poisoning in children. American Journal of Public Health 89 (11), 1690–1965.

United States Environmental Protection Agency Toxics Release Inventory, 2004. http://www.epa.gov/tri/. Accessed May.

USEPA-TRI, 2004.

Vojdani, A., Pangborn, J.B., Vojdani, E., Cooper, E.L., 2003. Infections, toxic chemicals and dietary peptides binding to lymphocyte receptors and tissue enzymes are major instigators of autoimmunity in autism. International Journal of Immunopathology and Pharmacology 16 (3), 189–199.

Yeargin-Allsopp, M., Rice, C., Karapurkar, T., Doernberg, N., Boyle, C., Murphy, C., 2003. Prevalence of autism in a US metropolitan area. Journal of the American Medical Association 289, 49–55.

EXHIBIT 6

Autism Spectrum Disorders in Relation to Distribution of Hazardous Air Pollutants in the San Francisco Bay Area

Gayle C. Windham,[1] Lixia Zhang,[2] Robert Gunier,[1] Lisa A. Croen,[3] and Judith K. Grether[1]

[1]Division of Environmental and Occupational Disease Control, California Department of Health Services, Richmond, California, USA; [2]Impact Assessment, Inc., La Jolla, California, USA; [3]Kaiser Permanente Medical Care Program Division of Research, Oakland, California, USA

OBJECTIVE: To explore possible associations between autism spectrum disorders (ASD) and environmental exposures, we linked the California autism surveillance system to estimated hazardous air pollutant (HAP) concentrations compiled by the U.S. Environmental Protection Agency.

METHODS: Subjects included 284 children with ASD and 657 controls, born in 1994 in the San Francisco Bay area. We assigned exposure level by census tract of birth residence for 19 chemicals we identified as potential neurotoxicants, developmental toxicants, and/or endocrine disruptors from the 1996 HAPs database. Because concentrations of many of these were highly correlated, we combined the chemicals into mechanistic and structural groups, calculating summary index scores. We calculated ASD risk in the upper quartiles of these group scores or individual chemical concentrations compared with below the median, adjusting for demographic factors.

RESULTS: The adjusted odds ratios (AORs) were elevated by 50% in the top quartile of chlorinated solvents and heavy metals [95% confidence intervals (CIs), 1.1–2.1], but not for aromatic solvents. Adjusting for these three groups simultaneously led to decreased risks for the solvents and increased risk for metals (AORs for metals: fourth quartile = 1.7; 95% CI, 1.0–3.0; third quartile = 1.95; 95% CI, 1.2–3.1). The individual compounds that contributed most to these associations included mercury, cadmium, nickel, trichloroethylene, and vinyl chloride.

CONCLUSIONS: Our results suggest a potential association between autism and estimated metal concentrations, and possibly solvents, in ambient air around the birth residence, requiring confirmation and more refined exposure assessment in future studies.

KEY WORDS: air toxics, autism, autism spectrum disorders, diesel, mercury, metals, neurodevelopment, neurotoxicants, solvents, vinyl chloride. *Environ Health Perspect* 114:1438–1444 (2006). doi:10.1289/ehp.9120 available via *http://dx.doi.org/* [Online 21 June 2006]

Autism is a serious neurodevelopmental disorder characterized by impairments in social interaction, verbal and nonverbal communication, and other restricted behaviors. The number of children reported with autistic spectrum disorders (ASDs) has increased dramatically during the last 10 years, but it is difficult to determine how much of this increase represents actual incidence and how much may be due to increased awareness and diagnosis; the causes remain largely unknown (Barbaresi et al. 2005; Croen et al. 2002a, 2002b; Newschaffer et al. 2005; Yeargin-Allsopp et al. 2003). Autism is believed to result from disruption of normal neurobiologic mechanisms primarily in the prenatal period and is widely recognized to have a strong genetic component, probably involving multiple gene loci. Nongenetic factors are also likely involved and may explain some of the increased prevalence. Medications such as thalidomide and valproic acid *in utero* have been linked to cases of autism (Moore et al. 2000; Rodier and Hyman 1998; Stromland et al. 1994). Maternal smoking during pregnancy has also been associated (Hultman et al. 2002), and there are case reports of children with both fetal alcohol syndrome and autism (Aronson et al. 1997). Other exogenous exposures known or suspected to interfere with neurodevelopment may also play a role in ASD etiology. Heavy metals such as lead and mercury have been relatively well studied in relation to impaired neurodevelopment (Bellinger et al. 1984; Burbacher et al. 1990; Grandjean et al. 1997; Mendola et al. 2002), but few studies have examined associations with autism. Compounds that interfere with the endocrine system may also play a role, particularly those affecting maternal thyroid hormones, which are critical to fetal brain development (Brouwer et al. 1998; London and Etzel 2000). In addition, prenatal exposure to some solvents has recently been associated with developmental delays in offspring (Laslo-Baker et al. 2004).

Hazardous air pollutants (HAPs), as defined by the Clean Air Act Amendments of 1990, are compounds associated with adverse health outcomes such as cancer and neurologic and developmental effects [U.S. Environmental Protection Agency (EPA) 1994]. For the most part, monitoring data on these pollutants have been limited. Therefore, the U.S. EPA developed a nationwide database with modeled annual average concentrations of HAPs (Rosenbaum et al. 1999). The estimated concentrations for several compounds, including some metals, exceed the health-based benchmark concentrations for chronic toxicity in both California and the United States (Morello-Frosch et al. 2000; Woodruff et al. 1998).

To track prevalence rates of autism and to provide descriptive data on the condition, surveillance has been instituted in several states. Coordinated by the Centers for Disease Control and Prevention (CDC), these programs have been organized into Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) and Autism and Developmental Disorders Monitoring (Rice et al. 2004; Yeargin-Allsopp et al. 2003). In six counties in the San Francisco Bay area, we are conducting multisource surveillance to ascertain ASD cases identified from clinical sources as well as from the Department of Developmental Services (DDS), which provides services for California residents with a variety of eligible developmental disabilities.

We conducted an exploratory case–control analysis linking our autism surveillance data to HAPs data for the San Francisco Bay area to examine the potential role of ambient chemical exposures during pregnancy or early life in ASD etiology.

Materials and Methods

Subjects. This study was approved by the California Committee for the Protection of Human Subjects. The population of interest included children born in 1994 to mothers resident at delivery in one of six San Francisco Bay area counties (Alameda, Contra Costa, Marin, San Francisco, San Mateo, and Santa Clara), representing approximately 80,000 births. Children with ASD were identified through the active surveillance conducted by

Address correspondence to G. Windham, Division of Environmental and Occupational Disease Control, California Department of Health Services, 850 Marina Bay Parkway, Building P, Richmond, CA 94804 USA. Telephone: (510) 620-3638. Fax: (510) 620-3720. E-mail: gwindham@dhs.ca.gov

We thank M. Falade and A. Hertz for geocoding, B. Hopkins and M. Anderson for autism data linkage and management, D. Smith for helpful comments, L. Lotspeich for expert clinical review, the California Centers for Autism and Developmental Disabilities Research and Epidemiology staff for data collection, and the California Department of Developmental Services regional centers and Kaiser Permanente Medical Care Program for provision of data on autism.

Funding was provided for data analyses by the Agency for Toxic Substances and Disease Registry and for surveillance and analyses by the Centers for Disease Control and Prevention, as well as by the California Department of Health Services.

The authors declare they have no competing financial interests.

Received 23 February 2006; accepted 21 June 2006.

California CADDRE, representing an approximate population-based series of affected children identifiable from existing records. At the time this study was conducted, the sources for case ascertainment were the DDS and the Kaiser Permanente Medical Care Program. Previous work has shown that DDS probably serves 75–80% of children with autistic disorder, or those on the more severe end of the autism spectrum (Croen et al. 2002a). From the DDS electronic database, California CADDRE staff originally identified clients with a diagnosis of autism or with mental retardation, epilepsy, or other developmental disorder with no known cause, before the child's ninth birthday. DDS records statewide were linked to birth certificate records to identify any cases born to mothers living in the six-county study area. Approximately 25% of births in these counties occur among Kaiser members, who are generally representative of the population except for the extreme ends of socioeconomic status (SES) (Krieger 1992). From Kaiser electronic files, children with an ASD diagnosis [Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV; 2000) code 299.00 or 299.80] before their ninth birthday were selected and then linked to birth certificates to identify resident births and duplicates with DDS. Trained CADDRE staff reviewed the DDS and Kaiser medical records of all identified children and abstracted standardized data for 341 with evidence of autism behaviors. About 21% were identified only in Kaiser, not DDS, and 25% were found in both systems. Final case status was determined by computer algorithm and several levels of expert review by a CADDRE principal investigator (J.G.) and/or a child psychiatrist with expertise in ASDs. This review process yielded 284 cases (83.3%) who met the stricter surveillance definition of ASD, having at least one of the following: *a*) a diagnosis of ASD from a qualified medical professional, *b*) qualification for special education under an autism exceptionality, or *c*) autistic behaviors that appear to meet DSM-IV criteria for a diagnosis of autistic disorder, Asperger's, or Pervasive Developmental Disorder not otherwise specified, per expert review.

We randomly selected control children for this study from the California 1994 linked birth–infant death certificate file with maternal residence at delivery in one of the six counties, matched to the original cases in a ratio of two to one by sex and month of birth (n = 682 for original cases). We subsequently excluded known deaths as well as controls served by DDS under other diagnoses (n = 8). We abstracted birth addresses from hard copies of the birth certificates, but several records were sealed because of adoption (n = 7). Demographic data and infant characteristics were obtained from the birth certificate.

We geocoded the birth addresses to obtain census tract for linkage to HAPs data. Using ArcGIS (version 9.0; ESRI Inc., Redlans, WA) and GDT version 11.1 street data for 2001 (Geographic Data Technology, Inc., Lebanon, NH), 95% were successfully geocoded via batch processing. The remaining 5% were manually geocoded. We then assigned a 1990 census tract based on the street segment where the geocoded addresses were located and the census tract boundaries (using Dynamap 2000 version 11.1 from GDT). Ten control addresses were not successfully assigned a tract, leaving 284 cases and 657 controls for our analysis.

Exposure assessment: hazardous air pollutant concentrations. The U.S. EPA estimates HAPs concentrations using a Gaussian air dispersion model that combines emissions inventories from mobile, point, and area sources with data on local meteorology, chemical decay rates, secondary formation, and deposition (Rosenbaum et al. 1999; Woodruff et al. 1998). Mobile sources include motor vehicles, airplanes, trains, and ships, whereas area sources include emissions from smaller stationary sources such as dry cleaners, gas stations, and residential use of products, and point sources are large industrial manufacturing facilities. Estimated concentrations are summed across these sources and background levels from "clean air locations" are added. Annual average HAPs concentration estimates are available at the U.S. census tract level for 1990 and 1996. We used the 1996 data because they were closer to the birth year of the subjects, and improvements had been made since 1990 in the emissions inventory data and the assumptions used in the dispersion model (U.S. EPA 2002a).

Because little prior information indicated which of the 33 compounds in the 1996 database might be related to autism, we took a broad approach, examining compounds that are recognized developmental toxicants or suspected neurologic toxicants and endocrine disruptors [California Environmental Protection Agency (CalEPA) 2003, 2005; Colborn et al.1993; Illinois Environmental Protection Agency (ILEPA) 1997; Keith 1997; National Institute for Occupational Safety and Health (NIOSH) 2001; U.S. EPA 2003]. We also considered chemicals that had been identified as contaminants of concern for an autism cluster investigation [Agency for Toxic Substances and Disease Registry (ATSDR) 2000], which resulted in adding only one chemical (chromium). We examined diesel particulate matter, although it does not specifically meet the above criteria, because diesel exhaust contains several compounds with relevant toxicity for autism, including arsenic, benzene, nickel, and polyaromatic hydrocarbons (PAHs). Thus, we examined 25 compounds with some toxicity potentially relevant to autism (Table 1).

We found that six compounds (Table 1) had a poor distribution and very little variability across the 1,228 census tracts in the study area, so we excluded them from further analyses. The concentrations of many of the remaining 19 compounds were highly correlated: 11 had Spearman correlation coefficients of ≥ 0.85 with more than one other compound. Because of the difficulty inherent in evaluating separate effects of these correlated compounds, we examined them in groups. Given toxicologic evidence, we grouped the compounds by mechanistic properties into developmental toxicants (n = 7) and endocrine disruptors (n = 10), which include some compounds in common (Table 1). We also grouped the compounds by structural properties into metals (n = 7), aromatic solvents (n = 5), and chlorinated solvents (n = 4), which are mutually exclusive (Table 1).

The mean concentrations of the compounds within a group varied by orders of magnitude (Table 1), so summing them to obtain an overall concentration for the group would underrepresent exposure to the chemicals with lower means. Therefore, we calculated an index score for each group. First, we categorized into quartiles the distributions of each individual compound across the census tracts in which controls were born. Then we assigned a level of one to four based on the quartile (low–high) and summed across the compounds included in each group to obtain an overall score for that chemical group, for each census tract. For example, with seven metals in the heavy metal group, the range of possible scores for a census tract was (7 × 1, if all low levels) to (7 × 4, if all high), or 7–28. The census tract group score was assigned to all cases and controls born in that tract. The mid-point of the score (e.g., 18 in the example above) generally corresponded well with the median of the score distribution, but because the distributions were non-normal, we categorized the scores into quartiles. We examined individual chemicals categorically as well, using the quartile cut points determined from the control distribution.

Statistical analyses. To maintain as large a sample size as possible, we did not exclude controls (n = 114) whose matched cases did not meet the surveillance criteria. Univariate analyses included examining quartile levels of chemicals and chemical groups described above by case–control status. For descriptive purposes, we also compared means of individual compounds by case–control status. We examined the potential covariates (maternal age, race, education, and parity; paternal race and age; low birth weight, preterm delivery, and child race) as categorical variables by the quartiles of the chemical group scores, as well

as by case–control status. We included those associated with chemical exposure as well as case status and those not highly redundant, such as parental and child race, in the final logistic regression models; these were child race, maternal age, and maternal education. The original matching variables did not meet these criteria, but we checked the effect of adding them to the models for the chemical groups; because it made little difference in the results, we did not maintain them in the final models. For the models, we calculated dummy variables for the third and fourth quartile exposure levels and combined the lower two quartiles as the referent group (below the median) to increase power and because there were generally not effects at the second quartile level. In some regression models we also included more than one chemical, or chemical group if they were mutually exclusive, to adjust for each other. Because a strict case–control match was not maintained, we did not use conditional logistic regression modeling except as a check on the findings from logistic regression models.

Table 1. Classification and distribution of concentrations of HAPS potentially relevant to autism.

Chemical groups	Suspected neurologic toxicant[a]	Recognized developmental toxicant[b]	Suspected endocrine toxicant[c]	Mean ± SD (μg/m³) Cases	Controls
Metals					
Arsenic[d]	X	X	X	0.0001 ± 0.00006	0.0001 ± 0.00005
Cadmium[d]	X	X	X	0.0001 ± 0.0002	0.0001 ± 0.0001
Chromium[d]				0.0044 ± 0.0057	0.0039 ± 0.0049
Lead[d]	X	X	X	0.0093 ± 0.0118	0.0082 ± 0.0092
Manganese	X			0.0032 ± 0.0017	0.0032 ± 0.0016
Mercury[d]	X	X	X	0.0008 ± 0.0019	0.0006 ± 0.001
Nickel	X			0.0043 ± 0.0059	0.0037 ± 0.0038
Aromatic solvents					
Benzene[d]	X	X	X	1.71 ± 0.62	1.66 ± 0.50
Ethyl benzene[d]	X		X	0.94 ± 0.44	0.91 ± 0.38
Styrene	X		X	0.10 ± 0.06	0.09 ± 0.05
Toluene[d]	X	X		6.98 ± 4.08	6.44 ± 3.00
Xylene[d]	X	X		3.77 ± 1.68	3.63 ± 1.46
Chlorinated solvents					
Methylene chloride[d]	X		X	0.68 ± 0.48	0.64 ± 0.35
Perchloroethylene[d]	X			0.61 ± 0.33	0.60 ± 0.34
Trichloroethylene[d]	X			0.19 ± 0.11	0.17 ± 0.08
Vinyl chloride[d]	X			0.02 ± 0.06	0.01 ± 0.02
Other HAPs					
Hydrazine	X		X	$1.29 \times 10^{-7} \pm 2.96 \times 10^{-7}$	$1.16 \times 10^{-7} \pm 2.39 \times 10^{-7}$
PAHs (7)[d]			X	0.0085 ± 0.0042	0.0086 ± 0.0041
Diesel PM[e]				3.37 ± 3.48	2.89 ± 2.35
Poor distributions[f]					
Carbon tetrachloride[d]	X		X	—	—
Chloroform[d]	X		X	—	—
Ethylene dibromide	X	X	X	—	—
Ethylene dichloride	X		X	—	—
Hexachlorobenzene	X	X	X	—	—
PCBs[d]	X	X	X	—	—

Abbreviations: PCBs, polychlorinated biphenyls; PM, particulate matter.
[a]Suspected neurologic toxicants (ATSDR 2000; CalEPA 2003; NIOSH 2001; U.S. EPA 2003). [b]Recognized developmental toxicants (CalEPA 2005). [c]Suspected endocrine disruptors (Colburn et al. 1993; ILEPA 1997; Keith 1997; NIOSH 2001). [d]Also on list of contaminants of concern for autism from ATDSR Brick Township Investigations (ATSDR 2000). [e]Diesel PM included because it contains compounds on the list including arsenic, benzene, nickel, and PAHs. [f]There was very little variability in estimated concentrations across most census tracts in study area, so these were excluded.

Table 2. Demographic characteristics of autism cases and live born–controls born in San Francisco Bay area, 1994.

Variable	Percent of cases (n = 284)	Percent of controls (n = 657)	Chi-square p-value
Male sex	84.9	81.0	0.15
Child's race			0.09
White	46.1	39.6	
Hispanic	18.1	26.3	
Other	35.8	34.1	
Maternal age (years)			0.09
< 25	19.0	25.6	
25–35	63.7	59.5	
≥ 35	17.3	14.9	
Maternal education			0.0001
< High school	9.9	17.7	
High school graduate	24.0	26.2	
Some college	33.9	21.5	
College graduate	32.2	34.6	
Parity			0.33
1	43.0	45.4	
2–3	51.1	46.6	
≥ 4	6.0	8.1	

Results

Compared with controls, cases were somewhat more likely to be white and less likely to be Hispanic, and to be born to mothers who were somewhat older and better educated (Table 2). This pattern also held for paternal age and education. The male:female ratio was 4:1, as expected from previous work (Croen et al. 2002b). Some of the demographic variables varied by exposure level, with nonwhites and younger and less-educated parents generally more likely to live in areas with higher exposure concentrations of both metals and solvents (data not shown).

The aromatic solvents and diesel particulate matter had the highest concentrations among the HAPs we examined (Table 1). The compounds with the widest range of concentrations among controls (e.g., standard deviation equal to or greater than the mean) tended to be the metals, as well as vinyl chloride and hydrazine (Table 1). The crude mean levels of the individual compounds were generally similar or slightly higher in cases compared with controls, particularly for diesel particulate matter and toluene (Table 1).

In logistic regression models that included a single chemical group, the adjusted odds ratios (AORs) for the mechanistic groups were slightly elevated for the fourth quartile levels (1.3 for endocrine disruptors and 1.4 for developmental toxicants (Table 3). By structural groups, AORs were elevated about 50% for fourth quartile levels of metals and chlorinated solvents (Table 3), and the AOR was also elevated for the third quartile level of metals. In models that adjusted for these groups together, the AORs were reduced for the solvents but were slightly higher for the metal group [metal AOR = 1.95; 95% confidence interval (CI), 1.23–3.09, and AOR = 1.74; 95% CI, 1.01–3.01 for the third and fourth quartile levels, respectively].

We looked further at the metal and chlorinated solvent groups to identify whether the observed associations were for the group in general or linked to specific compounds (Table 4). Among the chlorinated solvents, AORs for several compounds were slightly elevated at the third quartile, and AORs for trichloroethylene and vinyl chloride were significantly elevated at the fourth quartile

(AORs = 1.47 and 1.75, respectively). Among the metals, cadmium, mercury, and nickel had elevated AORs for the fourth quartiles (Table 4). Diesel particulate matter was examined separately and showed a similar magnitude of association (AOR = 1.44; 95% CI, 1.03–2.02). Diesel particulate matter, mercury, trichloroethylene and vinyl chloride showed elevated odds ratios (ORs) at the 90th percentile category as well (AORs = 1.6–1.9, data not shown).

As noted earlier, some of these compounds were strongly correlated to each other. Vinyl chloride was the least correlated with other compounds but showed some correlation with mercury (r = 0.70) and cadmium (r = 0.58), which were themselves correlated (r = 0.76). Nickel was most correlated with arsenic (r = 0.86) and cadmium (r = 0.77), and trichloroethylene was correlated with all three of these metals ($r \geq 0.77$). Concentrations of diesel particulate matter were also somewhat correlated with a few metals (r = 0.77–0.79, namely, arsenic, cadmium, and mercury). The aromatic solvents were all highly correlated with one another (r = 0.89–0.99) as well as to PAHs and manganese. We attempted to separate the mercury/cadmium relationship further by including both of these in one model; the AOR for the fourth quartile of mercury remained elevated (2.1; 95% CI, 1.25–3.50), but that for cadmium was reduced to below one. We examined their joint distribution by comparing subjects that had concentrations above the median for both compounds, or above the median for just one, with those with concentrations of both that were at or below the median. After adjustment, the AOR for the category of higher levels of both remained elevated at 1.75 (95% CI, 1.25–2.45), and the AORs for higher levels of either cadmium or mercury alone were in a similar range (AOR = 1.31; 95% CI, 0.77–2.25 and AOR = 1.55; 95% CI, 0.96–2.52, respectively). A similar analysis of mercury and vinyl chloride yielded AORs that were greatest for the higher mercury-only category (AOR = 2.04; 95% CI, 1.27–3.28), but in a similar range as higher vinyl chloride only (1.56, 95% CI, 0.95-2.56), or higher for both (AOR = 1.74; 95% CI, 1.24–2.45).

Discussion

These data suggest a potential association of autism with higher ambient air concentrations of metals and possibly chlorinated solvents in the geographic area of birth residence. There are several limitations to the exposure data to consider. Concentrations of many chemicals were correlated, so it was difficult to untangle specific chemicals of interest. Therefore, we combined levels of structurally similar chemicals using an index score similar to one used by others to examine mixtures (Swan et al. 2005). The concentrations represent modeled estimates of outdoor air levels based on chemical emissions in a geographic area, not actual personal measurements. The estimates used do not take into account mobility or specific maternal activities during pregnancy or child activities postnatally. Measurement studies have shown that personal exposures to volatile organic compounds (including the solvents) typically exceed measured outdoor air concentrations (Adgate et al. 2004; Sax et al. 2004), but that the U.S. EPA 1990 modeled HAPs concentrations were reasonable surrogates for personal exposure (Payne-Sturges et al. 2004). In general, the 1996 modeled estimates for most of the pollutants underestimate the measured ambient concentrations available from limited monitoring stations, particularly for the metals, although mercury was not examined (U.S. EPA 2002a). Our subjects were actually born in 1994, not in 1996 when the estimates were made, but based on available air monitoring data (California Air Resources Board 2005), it is unlikely that the relative rank of concentrations varied greatly in such a short time. Furthermore, we do not have addresses for the first trimester of pregnancy, which may be of most concern etiologically. Finally, the exposure estimates do not include other sources of chemical exposure such as occupational, active or passive smoking, or (particularly for metals) diet. These limitations lead to misclassification of exposure, but as this is unlikely to vary by case status, the effect estimates are probably shifted toward the null. Despite these limitations of the exposure data, the HAPs database has been used to investigate associations with other health outcomes, including childhood cancer (Reynolds et al. 2003) and reproductive outcomes (Vassilev et al. 2001).

This study had other minor limitations, including information on potential covariates available only from the birth certificate. However, several do reflect SES (e.g., education and race). These were considered likely *a priori* confounders because HAPs concentrations tend to be higher in lower SES census tracts (Morello-Frosch et al. 2002), whereas autism may be more likely to be detected among higher SES groups. Because so little is known about risks for autism, it is possible that uncontrolled confounding may partly explain

Table 3. Distribution and AOR[a] (95% CI) for autism risk by quartile[b] of hazardous air pollutant groups.

	HAP group level		
Group[c]	First and second quartiles no. of cases/controls Referent group	Third quartile no. of cases/controls AOR (95% CI)	Fourth quartile no. of cases/controls AOR (95% CI)
Mechanistic			
Endocrine disruptors	128/328	86/173	70/156
		1.33 (0.94–1.88)	1.28 (0.88–1.85)
Developmental toxicants	139/319	68/156	77/152
		1.13 (0.79–1.63)	1.40 (0.98–2.00)
Structural			
Aromatic solvents	148/328	64/173	72/156
		0.84 (0.59–1.20)	1.15 (0.80–1.65)
Chlorinated solvents	136/368	74/157	74/132
		1.33 (0.93–1.88)	1.55 (1.08–2.23)
Metals	123/348	79/141	82/168
		1.68 (1.17–2.41)	1.50 (1.05–2.12)

[a]Adjusted by logistic regression for maternal age, education and child race in separate models for each chemical. [b]Quartile cut points determined from distribution of index score among controls. [c]See text or Table 1 for definition of groups. Mechanistic groups overlap, e.g., some compounds are classified in both. Structural groups are mutually exclusive.

Table 4. AORs[a] (95% CIs) for upper quartiles of metals and chlorinated solvents by autism case–control status.

	Third quartile[b] AOR (95% CI)	Fourth quartile[b] AOR (95% CI)
Chemical chlorinated solvents		
Methylene chloride	1.50 (1.06–2.13)	1.37 (0.96–1.96)
Perchloroethylene	1.31 (0.93–1.84)	1.11 (0.78–1.59)
Trichloroethylene	1.37 (0.96–1.95)	1.47 (1.03–2.08)
Vinyl chloride	1.01 (0.69–1.47)	1.75 (1.25–2.43)
Metals		
Arsenic	1.07 (0.75–1.53)	1.28 (0.90–1.81)
Cadmium	1.43 (1.01–2.04)	1.54 (1.08–2.20)
Chromium	0.83 (0.58–1.20)	1.12 (0.79–1.58)
Lead	0.75 (0.52–1.09)	1.07 (0.76–1.51)
Manganese	1.12 (0.79–1.58)	1.09 (0.75–1.59)
Mercury	1.31 (0.91–1.88)	1.92 (1.36–2.71)
Nickel	1.11 (0.77–1.59)	1.46 (1.04–2.06)

[a]Adjusted by logistic regression for maternal age, education, and child race in separate models for each chemical. Reference is median or less. [b]Quartile cut points determined from distribution among controls.

the observed associations; for example, we had no data on maternal conditions or habits. The cases included in this study likely represent more severely affected children because of the nature of our case ascertainment sources. These children would be less likely to have diagnosis dependent on access and parental means. However, if children of lower SES who are more likely to be exposed were underrepresented in the case group, this could decrease the magnitude of effects observed.

Strengths of the study include availability of valid sources for identifying a population-based sample of cases and confirmation of diagnosis by review of records. Linkage to existing environmental exposure databases fulfills the mission of environmental health tracking programs, allowing relatively inexpensive study of retrospective exposure, which is not affected by recall bias. Examining 1990 HAPs levels in California, one study indicated that the urban areas, including the San Francisco Bay area, had the highest levels compared with other counties (Morello-Frosch et al. 2000), perhaps improving likelihood of detecting an association in this study. Although we examined many compounds, they were selected *a priori*, and the number with statistically significant associations was far greater than would be expected by chance. Our results were robust across various reanalyses of the data that included a less restrictive case definition or reassignment of census tract and exposure level, as well as when analyzed by conditional logistic regression using only individually matched controls.

There is limited prior work on environmental exposures that may be associated with autism in humans, but some plausibility for effects (reviewed by Allred and Wilbur 2002; Lawler et al. 2004; London and Etzel 2000). Prior studies have reported associations of autism with maternal smoking (Hultman et al. 2002), heavy alcohol consumption (Aronson et al. 1997), some prescription medications (Moore et al. 2000; Stromland et al. 1994), and parental occupations involving chemical exposures (reviewed by Allred and Wilbur 2002). These observations, combined with those from animal and neuroimaging studies, suggest that exposures early in gestation, around the time of neural tube closure, may be most critical (Rodier and Hyman 1998). A strong genetic component is indicated in the etiology of autism; it has been hypothesized this could involve susceptibility genes that, when combined with exposure, lead to this condition (London and Etzel 2000).

Of the postulated chemicals of interest in relation to autism, metals, particularly mercury, have generated the most attention. Several metals have been implicated in adverse neurodevelopmental outcomes in children, notably lead and mercury (ATSDR 1999a; Bellinger et al. 1984; Counter and Buchanan 2004; Mendola et al. 2002), with exposure to cadmium, arsenic, and chromium also of concern. Studies have found adverse effects of prenatal lead exposure on growth and development (Dietrich 1991), but little research has examined an association with autism (Eppright et al. 1996). Mercury is of concern because of evidence for neurotoxic effects and the fact that it has become ubiquitous in the global environment (Counter and Buchanan 2004; National Research Council 2000). Elemental mercury, released into the environment from the erosion of ores, industrial fossil fuel emissions (e.g., coal burning for power), and industrial waste, is the form of mercury represented in the HAPs database. The highest environmental exposure to mercury in humans currently is from methylmercury in the diet, but there is little study related to autism. Several incidents of widespread methyl mercury poisoning decades ago resulted in serious neurodevelopmental impairments in prenatally exposed children (Bakir et al. 1973; Tsubaki and Irukayama 1977). Ethylmercury, used in medical products and as a preservative (thimerosal) in common vaccines, contributes to total mercury levels in the blood, but there is little direct evidence of health effects, and expert reviews have concluded that vaccines are not associated with autism (Heron et al. 2004; Institute of Medicine 2004; Parker et al. 2004). Thimerosal has been removed from routine pediatric vaccines, but public debate and animal research continue (Burbacher et al. 2005; Geier and Geier 2003). Studies in animals have shown effects of elemental mercury that appear comparable to methylmercury or that are potentiated by joint exposure (ATSDR 1999a; Warfvinge 2000). Prenatal or early postnatal exposure to elemental mercury resulted in subtle behavioral changes in offspring in some studies and hyperactivity and alterations in spontaneous and learned behaviors that suggested deficits in adaptive functions (ATSDR 1999a). Although these data support our findings with elemental mercury, it would be most useful to have data on personal exposure to all forms of mercury from early pregnancy into childhood, which is logistically difficult. In addition to neurotoxic effects, some of the metals, including mercury, are suspected endocrine disruptors (Table 1), with effects on thyroid function also noted (ATSDR 1999a; Ellingsen et al. 2000; Takser et al. 2005).

A recent epidemiologic study (Palmer et al. 2006) linking Toxic Release Inventory (TRI) data on mercury to special education data in Texas reported a 61% increase in autism prevalence rates (or 17% adjusted) per 1,000 pounds of mercury released. The TRI industrial mercury emissions data are included as input data (from point sources) in the more complex model calculating HAPs concentrations that we used. Further interpretation and comparison of findings between our study and the Texas study are hampered by differences in the exposure measure (point source emissions vs. total concentrations used in this study), geographic scale (large counties vs. census tracts), and time period (year of school enrollment vs. year of birth).

Like mercury, cadmium is a recognized developmental toxicant with adverse effects on fetal growth and perhaps fetal viability at high doses (CalEPA 2005). There are few human data on neurodevelopmental effects, but in animals high prenatal levels were associated with changes in behavior and learning ability in offspring (ATSDR 1999b). Cadmium is also a suspected endocrine disruptor, with effects on steroidogenesis observed (Henson and Chedrese 2004).

Our results for aromatic solvents are difficult to interpret because the concentrations of these solvents were highly intercorrelated and tended to show less variation across the geographic area. We found moderate associations of autism with higher chlorinated solvent concentrations. These were lessened in models that adjusted for metals as well, but this could reflect some overadjustment. Vinyl chloride had the largest ORs of the chlorinated solvents and was not highly correlated to the others. Maternal solvent exposure has been associated with various adverse pregnancy outcomes, including spontaneous abortion, intrauterine growth retardation, and congenital malformations such as neural tube defects (ATSDR 1998; Bove et al. 1995; Cordier et al. 1997; McMartin et al. 1998; Windham et al. 1991; reviewed by Windham and Osorio 2004). A recent study followed offspring of women occupationally exposed to organic solvents and found that compared with unexposed children, these children obtained lower scores on subtests of intellectual, language, motor, and neurobehavioral functioning (Laslo-Baker et al. 2004). Together with our results, these suggest solvents should be examined further in relation to autism.

The moderate association we found with higher diesel particulate matter levels may in part be due to some correlation with metals. Nevertheless, studies of reproductive outcomes in New Jersey found the highest tertile level of airborne polycyclic organic matter, a related class of particulate matter, was associated with risks increased 20–30% for preterm birth, low birth weight, and fetal death (Vassilev et al. 2001). Results of a study of diesel exhaust exposure in neonatal rats suggested permanent alterations in both learning ability and activity, indicating that the significance to humans should be pursued further (U.S. EPA 2002b). Other animal studies have indicated potential endocrine-disrupting

effects of prenatal exposure to diesel exhaust (Watanabe and Kurita 2001) and increased indices of inflammation in brains of mice exposed to airborne particulate matter (Campbell et al. 2005).

Environmental exposures occur in mixtures determined by emissions sources, so it is difficult to disentangle effects of specific compounds or groups of compounds, and adverse health effects may be potentiated by joint exposures. However, when we examined joint exposure of mercury with cadmium or vinyl chloride, clear interaction was not noted. Within the six counties we studied, San Francisco County had by far the highest mean levels for six representative compounds we compared (mercury, cadmium, diesel particulate matter, methylene chloride, toluene, and vinyl chloride) and also had a higher ratio of cases to controls than overall (0.71 vs. 0.43). In contrast, Marin County, with the lowest levels of these chemicals, had a much lower ratio (0.14). However, these patterns may reflect other factors, including diagnostic differences or care-seeking behavior.

Conclusions

Results of this semiecologic study suggest that living in areas with higher ambient levels of HAPs, particularly metals and chlorinated solvents, during pregnancy or early childhood, may be associated with a moderately increased risk of autism. These findings illuminate the need for further scientific investigation, because although potentially biologically plausible they are preliminary and require confirmation. The autism surveillance network funded by the CDC and the availability of HAPs data nationwide provide the opportunity for similar linkage studies to be conducted in other locations, and we plan to look at 1996 autism surveillance data when available. Additional sources or refinement of such data may be available in different states or regions and could also be examined. More complex etiologic studies with measurements of individual level exposures to multiple compounds by various pathways (air, water, diet), combined with genetic information, will be important to further our understanding of the potential contribution of environmental exposures to the development of autism.

References

Adgate JL, Church TR, Ryan AD, Ramachandran G, Fredrickson AL, Stock TH, et al. 2004. Outdoor, indoor, and personal exposures to VOCs in children. Environ Health Perspect 112:1386–1392.

Allred M, Wilbur S. 2002. Hazardous substance exposures and autism. In: Impact of Hazardous Chemicals on Public Health, Policy, and Service (DeRosa CT, Holler JS, Mehlman MA, eds). Advances in Modern Toxicology, Vol. 26. Princeton, NJ:International Toxicology Books, Inc., 453–474.

Aronson M, Hagver B, Gillberg C. 1997. Attention deficits and autistic spectrum problems in children exposed to alcohol during gestation: a follow-up study. Dev Med Child Neurol 39:583–587.

ATSDR. 1998. A Case-Control Study of Neural Tube Defects and Drinking Water Contaminants. Atlanta, GA:Agency for Toxic Substances and Disease Registry.

ATSDR. 1999a. Toxicological Profile for Mercury. Atlanta, GA:Agency for Toxic Substances and Disease Registry.

ATSDR. 1999b. Toxicological Profile for Cadmium. Atlanta, GA:Agency for Toxic Substances and Disease Registry.

ATSDR. 2000. Division of Health Assessment and Consultation. Public Health Assessment, Brick Township Investigation, Appendix A—Contaminants of Concern. Atlanta, GA:Agency for Toxic Substances and Disease Registry. Available: http://www.atsdr.cdc.gov/HAC/PHA/bri/bri_p2.html [accessed 2 June 2004].

Bakir F, Kamluji SF, Amin-Zaki L, Murtadha M, Khalidi A, Al Rawi NY, et al. 1973. Methylmercury poisoning in Iraq. Science 181:230–241.

Barbaresi WJ, Katusic SK, Colligan RC, Weaver AL, Jacobsen SJ. 2005. The incidence of autism in Olmsted County, Minnesota, 1976–1997. Arch Pediatr Adolesc Med 159:37–44.

Bellinger DC, Needleman HL, Leviton A, Waternaux C, Rabinowitz MB, Nichols ML. 1984. Early sensory-motor development and prenatal exposure to lead. Neurobehav Toxicol Teratol 6:387–402.

Bove FJ, Fulcomer MC, Klotz JB, Esmart J, Dufficy EM, Savrin JE. 1995. Public drinking water contaminations and birth outcomes. Am J Epidemiol 141:850–862.

Brouwer A, Morse DC, Lans MC, Schuur AG, Murk AJ, Klasson-Wehler E, et al. 1998. Interactions of persistent environmental organohalogens with the thyroid hormone system: mechanisms and possible consequences for animal and human health. Toxicol Ind Health 14:59–84.

Burbacher TM, Rodier PM, Weiss B. 1990. Methylmercury developmental neurotoxicity: a comparison of effects in humans and animals. Neurotoxicol Teratol 12:191–202.

Burbacher TM, Shen DD, Liberato N, Grant KS, Cernichiari E, Clarkson T. 2005. Comparison of blood and brain mercury levels in infant monkeys exposed to methylmercury or vaccines containing thimerosal. Environ Health Perspect 113:1015–1021.

CalEPA. 2003. Office of Environmental Health Hazard Assessment. Air Toxics Hot Spots Program Risk Assessment Guidelines. Part III. Technical Support Document. Determination of Noncancer Chronic Reference Exposure Levels, Sacramento, CA:California Environmental Protection Agency. Available: http://www.oehha.ca.gov/air/chronic_rels/index.html [accessed 19 May 2004].

CalEPA. 2005. Proposition 65 List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity, Sacramento, CA:California Environmental Protection Agency. Available: http://www.oehha.ca.gov/prop65/prop65_list/files/P65single3405.pdf [accessed 19 May 2004].

California Air Resources Board. 2005. Air Quality, Emissions and Modeling Section. California Toxics Air Quality Data for 1994–1996. Sacramento, CA. Available: http://www.arb.ca.gov/adam/toxics/toxics.html [accessed 9 September 2004].

Campbell A, Oldham M, Becaria A, Bondy SC, Meacher D, Sioutas C, et al. 2005. Particulate matter in polluted air may increase biomarkers of inflammation in mouse brain. Neurotoxicology 26(1):133–140.

Clean Air Act Amendments of 1990. 1990. Public Law 101-549.

Colborn T, vom Saal FS, Soto AM. 1993. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. Environ Health Perspect 101:378–384.

Cordier S, Bergeret A, Goujard J, Ha M-C, Ayme S, Bianchi F, et al. 1997. Congenital malformations and maternal occupational exposure to glycol ethers. Epidemiology 8:355–363.

Counter SA, Buchanan LH. 2004. Mercury exposure in children: a review. Toxicol Applied Pharmacol 198:209–230.

Croen LA, Grether JK, Hoogstrate J, Selvin S. 2002a. The changing prevalence of autism in California. J Autism Dev Disord 32:207–215.

Croen LA, Grether JK, Selvin S. 2002b. Descriptive epidemiology of autism in a California population: who is at risk? J Autism Dev Disord 32:217–224.

Diagnostic and Statistical Manual of Mental Disorders. 2000. 4th ed. Arlington, VA: American Psychiatric Publishing.

Dietrich KN. 1991. Human fetal lead exposure: intrauterine growth, maturation, and postnatal neurobehavioral development. Fundam Appl Toxicol 16:17–19.

Ellingsen DG, Efskind J, Haug E, Thomasses Y, Martinsen I, Gaarder PI. 2000. Effects of low mercury vapour exposure on the thyroid function in chloralkali workers. J Appl Toxicol 20:483–489.

Eppright TD, Sanfacon JA, Horwitz EA. 1996. Attention deficit hyperactivity disorder, infantile autism and elevated blood-lead: a possible relationship. Mo Med 93(3):136–138.

Geier DA, Geier MR. 2003. An assessment of the impact of thimerosal on childhood neurodevelopmental disorders. Pediatr Rehabil 6(2):97–102.

Grandjean P, Weihe P, White RF, Debes F, Araki S, Yokoyama K, et al. 1997. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. Neurotoxicol Teratol 19:417–428.

Henson MC, Chedrese PJ. 2004. Endocrine disruption by cadmium, a common environmental toxicant with paradoxical effects on reproduction. Exp Biol Med 229(5):383–392.

Heron J, Gloding J, and the ALSPAC Study Team. 2004. Thimerosal exposure in infants and developmental disorders: a prospective cohort study in the United Kingdom does not support a causal association. Pediatrics 114:557–583.

Hultman CM, Sparen P, Cnattingius S. 2002. Perinatal risk factors for infantile autism. Epidemiology 13:417–423.

ILEPA. 1997. Table 1: Preliminary list of chemicals associated with endocrine system effects in animals and humans or in vitro. In: Endocrine Disruptors Strategy. Springfield, IL:Illinois Environmental Protection Agency.

Institute of Medicine. 2004. Immunization safety review committee. Vaccines and Autism. Washington, DC:Institute of Medicine.

Keith LH, ed. 1997. Environmental Endocrine Disruptors. NY:John Wiley & Sons.

Krieger N. 1992. Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. Am J Public Health 82(5):703–710.

Laslo-Baker D, Barrera M, Knittel-Keren D, Kozer E, Wolpin J, Khattak S, et al. 2004. Child neurodevelopmental outcome and maternal occupational exposure to solvents. Arch Pediatr Adolesc Med 158:956–961.

Lawler CP, Croen LA, Grether JK, Van de Water J. 2004. Identifying environmental contributions to autism: provocative clues and false leads. Ment Retard Dev Disabil Res Rev 10:292–302.

London E, Etzel RA. 2000. The environment as an etiologic factor in autism: a new direction for research. Environ Health Perspect 108(suppl 3):401–404.

McMartin KI, Chu M, Kopecky E, Einarson TR, Koren G. 1998. Pregnancy outcome following maternal organic solvent exposure: a meta-analysis of epidemiologic studies. Am J Ind Med 34:288–292.

Mendola P, Selevan SF, Gutter S, Rice D. 2002. Environmental factors associated with a spectrum of neurodevelopmental deficits. Ment Retard Dev Disabil Res Rev 8:188–197.

Moore SJ, Turnpenny P, Quinn A, Glover S, Lloyd DJ, Montgomery T, et al. 2000. A clinical study of 57 children with fetal anticonvulsant syndrome. J Med Genet 37:489–497.

Morello-Frosch R, Pastor M, Porras C, Sadd J. 2002. Environmental justice and regional inequality in southern California: implications for future research. Environ Health Perspect 110(suppl 2):149–154.

Morello-Frosch RA, Woodruff TJ, Axelrad DA, Caldwell JC. 2000. Air toxics and health risks in California: the public health implications of outdoor concentrations. Risk Anal 20:273–291.

National Research Council. 2000. Committee on the toxicological effects of methylmercury. Toxicological Effects of Methylmercury. Washington, DC:National Academy Press.

Newschaffer CJ, Falb MD, Gurney JG. 2005. National autism prevalence trends from United States special education data. Pediatrics 115:e277–e282.

NIOSH. 2001. Registry of Toxic Effects of Chemical Substances. Cincinnati, OH:National Institute for Occupational Safety and Health. Available: http://www.cdc.gov/niosh/rtecs.html [accessed 19 May 2004].

Palmer RF, Blanchard S, Stein Z, Mandell D, Miller C. 2006. Environmental mercury release, special education rates, and autism disorder: an ecological study of Texas. Health Place 12:203–209.

Parker SK, Schwartz B, Todd J, Pickering LK. 2004. Thimerosal-containing vaccines and autistic spectrum disorder: a critical review of published original data. Pediatrics 114:793–804.

Payne-Sturges DC, Burke TA, Breysse P, Diener-West M, Buckley TJ. 2004. Personal exposure meets risk assessment:

a comparison of measured and modeled exposures and risks in an urban community. Environ Health Perspect 112:589–598.

Reynolds P, Von Behren J, Gunier RB, Goldberg DE, Hertz A, Smith DF. 2003. Childhood cancer incidence rates and hazardous air pollutants in California: an exploratory analysis. Environ Health Perspect 111:663–668.

Rice C, Schendel D, Cunniff C, Doernberg N. 2004. Public health monitoring of developmental disabilities with a focus on the autism spectrum disorders. Am J Med Genet C Semin Med Genet 125(1):22–27.

Rodier PM, Hyman SL. 1998. Early environmental factors in autism. Ment Retard Dev Disabil Res Rev 4:121–128.

Rosenbaum AS, Axelrad DA, Woodruff TJ, Wei Y-H, Ligocki MP, Cohen JP. 1999. National estimates of outdoor air toxics concentrations. J Air Waste Manag Assoc 49:1138–1152.

Sax SN, Bennett DH, Chillrud SN, Kinney PL, Spengler JD. 2004. Differences in source emission rates of volatile organic compounds in inner-city residences of New York City and Los Angeles. J Expo Anal Environ Epidemiol 14(suppl 1):S95–S109.

Stromland K, Nordin V, Miller M, Akerstrom B, Gillberg C. 1994. Autism in thalidomide embryopathy: a population study. Dev Med Child Neurol 36:351–356.

Swan SH, Main KM, Liu F, Stewart SL, Kruse RL, Calafat AM, et al. 2005. Decrease in anogenital distance among male infants with prenatal phthalate exposure. Environ Health Perspect 113:1056–1061.

Takser L, Mergler D, Baldwin M, de Grosbois S, Smargiassi A, Lafond J. 2005. Thyroid hormones in pregnancy in relation to environmental exposure to organochlorine compounds and mercury. Environ Health Perspect 113:1039–1045.

Tsubaki T, Irukayama K, eds. 1977. Minamata Disease: Methylmercury Poisoning in Minamata and Niigata, Japan. New York:Elsevier.

U.S. EPA. 1994. Technical Background Document to Support Rulemaking Pursuant to Clean Air Act Section 112(g): Ranking of Pollutants with Respect to Human Health. EPA-450/3-92-010. Research Triangle Park, NC:U.S. Environmental Protection Agency.

U.S. EPA (U.S. Environmental Protection Agency). 2002a. Office of Air and Radiation. National-Scale Air Toxics Assessment, 1996 Hazardous Air Pollutant Concentrations by Census Tract. Available: http://www.epa.gov/ttn/atw/nata [accessed 16 January 2004].

U.S. EPA. 2002b. Office of Research and Development. Health Assessment Document for Diesel Engine Exhaust. EPA/600/8-90/057F. Washington, DC:U.S. Environmental Protection Agency.

U.S. EPA (U.S. Environmental Protection Agency). 2003. Air Risk Information Support Center. Health Effects Notebook for Hazardous Air Pollutants. Available: http://www.epa.gov/ttnatw01/hlthef/hapindex.html [accessed 26 May 2004].

Vassilev ZP, Robson MG, Klotz JB. 2001. Outdoor exposure to airborne polycyclic organic matter and adverse reproductive outcomes: a pilot study. Am J Ind Med 40:255–262.

Warfvinge K. 2000. Mercury distribution in the neonatal and adult cerebellum after mercury vapor exposure of pregnant squirrel monkeys. Environ Res 83:93–101.

Watanabe N, Kurita M. 2001. The masculinization of the fetus during pregnancy due to inhalation of diesel exhaust. Environ Health Perspect 109:111–119.

Windham GC, Osorio AM. 2004. Female reproductive toxicology. In: Occupational and Environmental Medicine (LaDou J, ed). 3rd ed. Norwalk, CT:Appleton and Lange, Inc., 397–413.

Windham GC, Shusterman D, Swan SH, Fenster L, Eskenazi B. 1991. Exposure to organic solvents during pregnancy and adverse pregnancy outcome. Am J Ind Med 20:241–259.

Woodruff TJ, Axelrad DA, Caldwell J, Morello-Frosch R, Rosenbaum A. 1998. Public health implications of 1990 air toxics concentrations across the United States. Environ Health Perspect 106(5):245–251.

Yeargin-Allsopp M, Rice C, Karapurkar T, Doernberg N, Boyle C, Murphy C. 2003. Prevalence of autism in a US metropolitan area. JAMA 289:49–55.

EXHIBIT 7

Int. J. Cancer: **108,** 907–911 (2004)

Publication of the International Union Against Cancer

EXPOSURE TO CEMENT DUST, RELATED OCCUPATIONAL GROUPS AND LARYNGEAL CANCER RISK: RESULTS OF A POPULATION BASED CASE-CONTROL STUDY

Andreas DIETZ[1],* Heribert RAMROTH[2], Tobias URBAN[3], Wolfgang AHRENS[4] and Heiko BECHER[3]

[1]*Department of Otolaryngology, Head and Neck Surgery, University of Heidelberg, Heidelberg, Germany*
[2]*Division of Clinical Epidemiology, German Cancer Research Centre, Heidelberg, Germany*
[3]*Department of Tropical Hygiene and Public Health, University of Heidelberg, Heidelberg, Germany*
[4]*Bremen Institute for Prevention Research and Social Medicine (BIPS), Bremen, Germany*

A population-based case-control study was performed in the Rhein-Neckar region, Germany, to evaluate occupational risk factors for the development of laryngeal cancer ("Rhein-Neckar-Larynx Study"). Between May 1998 and December 2000, 257 patients (236 males, 21 females), aged 37–80, with histologically confirmed laryngeal cancer, as well as 769 population control persons (702 males, 67 females), were included (1:3 frequency matched by age and sex). History of occupational exposures, as well as other risk factors (tobacco, alcohol), was obtained with face-to-face interviews using a detailed standardized questionnaire. The complete individual work history was assessed. A detailed assessment of work conditions was obtained by job-specific questionnaires (JSQs) for selected jobs known to be associated with exposure to potential laryngeal carcinogens. Estimates for total exposure hours by substance were calculated based on JSQs. Published occupational hygiene data were used to infer semiquantitative scores of exposure intensity for specific job tasks. After adjustment for tobacco and alcohol intake, a significant elevated odds ratios (OR) could be demonstrated for persons that were exposed to cement during their work as building and construction workers. An OR of 2.42 was calculated for workers of the high exposed subgroup (95% confidence interval: 1.14-5.15; $p < 0.001$). Smoking was the main confounding factor because the unadjusted cement OR of 3.20 dropped down to 2.42 after adjustment for tobacco intake. We conclude that there is good evidence for cement dust exposure acting as a tobacco, alcohol and asbestos independent risk factor for laryngeal carcinoma. Our study gives a base for further toxicologic investigations on this topic.

Key words: *laryngeal carcinoma; occupational exposure; construction industry; epidemiology; cement dust*

Squamous cell carcinoma of the larynx (yearly incidence about 10/100,000 in Germany) is the most common malignant tumour of the upper aerodigestive tract in Caucasians. Average prognosis ranges between 80% 5-year survival for glottis, 68% for supraglottis and 53% for subglottis carcinoma.[1] Cure rates for early glottis cancer are nearly 100% but many patients suffer from advanced disease at date of the first diagnosis. Current therapies for advanced tumour stages still includes radical laryngectomy followed by radiotherapy, with severe implications for quality of life in many cases. Therefore, prevention and determination of risk factors is of very high interest.

Tobacco smoking represents a major risk factor for laryngeal cancer, as well as alcohol consumption, which has been consistently demonstrated by a variety of epidemiologic studies.[2] According to findings from research on genotoxicity and occupational factors, it has been suggested that 10% of all carcinomas in Germany and the US are related to exposure to hazards in the occupational environment.[3,4] Comprehensive epidemiologic research over the last 40 years has identified certain occupational factors that are associated with the risk for developing laryngeal cancer, such as asbestos,[5,6] mineral coal products, mineral oil,[7,8] fossil fuels,[9] coking plant emissions and other polycyclic aromatic compounds (PAH),[10] ionising radiation, mustard gas, chromium-VI-compounds, wood dust,[11,12] nickel compounds, sulfuric acid, isopropylalcohol and bis-chloromethylether[2] and emissions in the paper-,[13] textile-,[14,15] leather-[16] and rubber industries.[17,18] Finally, painters and varnishers probably have an elevated risk for laryngeal carcinoma. Paints are very heterogeneous compositions containing some carcinogenic hazards, e.g., chromium-VI-compounds.[19]

In addition, the environment of building and construction workers might also cause a higher risk of developing laryngeal carcinoma. In several studies (predominantly case-control studies) significant increased risks (adjusted for tobacco and alcohol effects) were found for construction dust.[7,20–23] Construction dust contains many different substances, such as asbestos, mineral fibers, sand or metal powders, tar, bitumen and cement dusts. The question of which single agent is responsible for the elevated laryngeal cancer risk remains unanswered, although some studies could identify cement dust as the main candidate. In a German case-control study,[24] cement dust was associated with a relative risk (RR) of 2.4, which could be further differentiated into exposure time dependent increased risks (duration of exposure 5–20 years: RR 2.9; 20–40 years: RR 5.5; > 40 years: RR 6.3). After adjustment for tobacco and alcohol (ever exposed) the RR remained significantly elevated at 1.8 ($p = 0.03$). The results from a French case-control study demonstrated that cancer of the supraglottic larynx has been associated with exposure to cement dust (odds ratio [OR] = 4.2; 95% confidence interval [CI] = 1.1–16.4).[25] Furthermore, an association between cement dust and gastrointestinal cancer has been shown.[26]

Despite the obvious need to clarify the role of cement dust as a potential risk factor for laryngeal carcinoma, only a few studies have focused on this issue. Thus, we performed a comprehensive population-based case-control study in Germany. Our study aimed to investigate and narrow down the supposed cement-associated risk for laryngeal cancer (*inter alia*) after adjustment for main confounding factors.

MATERIAL AND METHODS

Our study was conducted in the Rhein-Neckar-Odenwald Region of southwest Germany, with a population of about 2.7 mil-

Grant sponsor: Bundesministerium für Bildung und Forschung (BMBF); Grant number: 01GB 9702/3.

*Correspondence to: Universitäts-Hals-Nasen-Ohrenklinik, Im Neuenheimer Feld 400, 69120 Heidelberg 69120, Germany.
Fax: +06-221-566706. E-mail: Andreas_Dietz@med.uni-heidelberg.de

Received 7 May 2003; Revised 24 September 2003; Accepted 1 October 2003

DOI 10.1002/ijc.11658

lion. Within this region between May 1, 1998 and December 31, 2000, nearly all incident cases (response rate 96%) of histologically confirmed squamous cell carcinoma of the larynx (ICD-9-Nr. 161.0–161.9) were recruited ($n = 257$) and frequency matched 1:3 (by age, gender and location) with population controls ($n = 769$) randomly drawn from population registries. Further inclusion criteria were age less than 80 years, German nationality and mental ability for the interview. Cases were recruited at the Department of Otolaryngology, Head and Neck Surgery university hospitals of Heidelberg and Mannheim and town hospitals of Ludwigshafen, Darmstadt and Heilbronn. These hospitals exclusively treat patients with laryngeal cancer within our study region. Local practitioners were additionally contacted to check for possible cases sent to other more distant clinics and to verify complete case ascertainment. The list of population controls was assembled by the town registration offices of our study region and kept at the centre study office. The procedure for drawing population controls from various population registries in our study has been previously described by Ramroth *et al.*[27] Altogether, the extent of the control random sample selected by the several registration offices was 32,435 persons. Out of this sample, 1,233 eligible persons were randomly chosen according to the age and sex distribution of the cases. Finally, 769 (response rate: 62.4%) were included in our study, which is rather high considering the fact that blood samples were required by the participants and a special technique of recruitment was performed (e.g., invitation to come to the clinics for interview).

The ages of study participants was between 40 and 75 years. Distribution of sex in cases was 236 men and 21 women. Family status was comparable in cases and controls.

Occupational exposures, as well as other risk factors, were obtained by face-to-face interviews using a detailed standardised questionnaire. Before the start of our study, 5 female interviewers, who were exclusively employed for our study, underwent special questionnaire training. The interview was conducted usually before start of therapy. The interviews of cases and controls were performed predominantly in the hospitals (better facilities for taking blood in controls) mentioned above, and some were conducted in the participant's home. Table I shows the distribution of our study sample.

The assessment of occupational exposure was derived from 3 different sources of the questionnaire: a detailed occupational history of all jobs held for at least 6 months, an exposure check-list for known and suspected carcinogens of the respiratory tract, and 34 job-specific supplementary questionnaires (JSQ) addressing specific exposures in job—or branch of industry—oriented questions. Estimates for lifetime exposure hours by substance were calculated based on JSQs. Published occupational hygiene data were used to infer semi-quantitative scores of exposure intensity for specific job tasks. The quantification procedure was a modification of methods described elsewhere,[28] and the performance of this method with respect to asbestos has been evaluated.[29] Industries and job titles were coded according to the standard classifications provided by Statistisches Bundesamt (1993)[30] and the ILO (1968).[31] The analysis of the job history was based on these codes, which were grouped into 32 and 21 categories, respectively, on an ever-never-basis and by duration as described before.[32]

Additionally a list of agent exposures was checked in every study attendant. Further concentrated attention was paid to consumption of tobacco and alcohol, passive smoking, family health, nutrition, social status and special personal environmental factors other than occupation.

To narrow down data of the individual cement dust exposure, a validation study was performed in exposed cases and controls. A special cement questionnaire asked for ceil techniques; grouts and plaster materials like mortar containing lime, unslaked or slaked lime and gypsum; the way of processing cement-based products on site and the detailed daily direct or indirect cement dust exposure. For every kind of job, associated cement exposure life working hours were calculated by different indices. In case of parallel exposure, the maximum exposure level for a given time period was taken. Rating for cement exposure was done by distinguishing between nonexposure ("0"), middle and high exposure dependent on the median of the controls cement exposure duration.

Another expected confounding factor in analysis of cement associated cancer risk is constituted by asbestos, in particular asbestos cement exposure. For this reason, an exact assessment of exposure to the diverse modifications of asbestos was done. The questionnaire and the JSQs contained the following topics: direct handling/processing of asbestos, using asbestos heat protecting or isolation, contact with asbestos materials and employment in the asbestos industry. Furthermore, asbestos environment was checked in the list of hazardous substances. In consideration of these data, calculation of asbestos life working hours was performed in the same way as was done for cement exposure.

All ORs given are based on a conditional logistic regression model conditioned on a sex × age classification (5-year age groups).[33] Adjustment for smoking, alcohol consumption and social status was performed as indicated in the tables. To assess the magnitude of confounding, OR estimates with and without adjustment are presented; however, the interpretation of the occupational risks is based on the adjusted values. The statistical software package SAS (PROC PHREG) was used.

Smoking was considered as the cumulative number of cigarettes smoked (pack years [py]; 1 py ≅ 20 cigarettes/day for 1 year ≅ 7,300 cigarettes). Cigars, cigarillos and pipes were added according to their weight relative to that of cigarettes. It was included as a log-transformed continuous variable (log(py+1)). Residual confounding through smoking was minimized by comparing the results using other transformations of the smoking dose, including a categorization into 6 categories (0, > 0–10, > 10–20, > 20–30, > 30–40, > 40 py). The transformation used here gave the best fit and also, in most cases, the maximally reduced estimates for the occupational variables of interest. Time since smoking cessation was included as binary variable "having stopped smoking at least 2 years before diagnosis/before interview." Average daily alcohol consumption was included as a continuous variable.

Daily alcohol consumption was calculated from the alcohol data obtained by the interview (daily, weekly and monthly alcohol consumption 10 years before interview for all common alcoholic beverages), assuming the following ethanol content: beer 5%; wine, fruitwine or sparkling wine 10%; aperitif and liquors 20% and spirits 40%. Average daily alcohol consumption was included as continuous variable in the final model because it gave the best fit. Again, other methods for alcohol adjustment using categories (< 25 g, 20–50 g, 50–75 g, > 75 g ethanol per day) were also investigated. School education was considered as a surrogate variable for social status in 3 levels according to the German educational system (9 years and less "Hauptschule", 10 years "mittlere Reife" and more than 10 years ("(Fach)Hochschulreife").

TABLE I – STUDY SAMPLE (NUMBER OF PARTICIPANTS) AND LOCATION OF INTERVIEW AT THE DEPARTMENTS OF OTOLARYNGOLOGY, HEAD AND NECK SURGERY OF THE TOWN HOSPITALS OF DARMSTADT, HEILBRONN, LUDWIGSHAFEN AND THE UNIVERSITY HOSPITALS OF HEIDELBERG, MANNHEIM

	Darmstadt	Heidelberg	Heilbronn	Ludwigshafen	Mannheim	At home	Sum
Controls	112	234	91	113	4	215	769
Cases	43	61	22	53	78	0	257
Sum	155	295	113	167	82	215	1,026

The scientific nature of our study was explained to all the patients and they gave their informed consent to participate in this investigation. The protocol was approved by the Ethical Committee of the University of Heidelberg.

RESULTS

Before presentation of the results regarding environmental risk factors for laryngeal carcinoma, the main confounding factors in our study should be described. Cigarette smoking was the outstanding risk factor for laryngeal carcinoma in the Rhein-Neckar-Larynx Study. Only 2.1% of male and 19.0% of female cases were never smokers compared to 23.8% of male and 53.7% of female controls, respectively. The OR for 0–10 py was 3.9 (95% CI: 1.5–9.7), increasing to 32.8 (95% CI: 15.1–71.0) in the group of heavy smokers (> 40 py) after adjustment for alcohol. Analysis of chronic alcohol consumption showed ORs of up to 2.4 in the highest group consuming more than 75 g alcohol per day (adjusted for tobacco intake, 95% CI: 1.5–3.6). More detailed data about larynx cancer risk associated to tobacco and alcohol of our study are publicized elsewhere. Socioeconomic status, assessed as described in the Material and Methods section, showed differences between cases and controls. Among males, the differences between cases and controls among the first, second and third categories were 87.3% and 62.1%, 6.8% and 15.0% and at least 5.9% and 22.9%, respectively.

Regarding traditional industries, in our study, the group of building and construction workers showed evidence of risk for laryngeal cancer. There were 103 (40.1%) cases and 163 (17.7%) controls who ever had worked as building or construction workers. This industry had an OR of 2.6 without adjustment and 2.2 (95% CI: 1.55–3.14) after adjustment for the confounders tobacco and alcohol. Considering the industry in which employment was longest time of life, building and construction work demonstrated an adjusted larynx carcinoma risk of 1.9 (95% CI: 1.2–3.0).

Further analysis for single substances focused on cement dust. According to the JSQs, 14.8% of male cases and 5.1% of male controls were exposed to cement dust (female cases did not show any exposure to cement dust). With regard to the list of hazardous substances, 23.3% of cases showed cement exposure compared to 14.4% of the controls. Cement exposure duration showed 8.1% of cases compared to 2.7% of controls to be highly exposed with a life working hours account of more than 3,000 hr (Table II).

After adjustment for tobacco, alcohol intake and socioeconomic status, statistically significant elevated ORs could be demonstrated for persons ever being exposed to cement in their life. Based on categorisation in no, middle and high exposure, no clear dose response was observed. However the calculated ORs are compatible with increasing risk by cement dust exposure. Smoking is the main confounding factor considering the unadjusted cement OR of 3.2 decreasing to 2.4 after tobacco adjustment (Table II).

No exposure to asbestos was reported by 75.0% of male cases and 85.2% of male controls (all female participants were not exposed). All ORs related to the topics of the asbestos-JSQs did not reach significantly elevated levels after adjustment for tobacco and alcohol. The high exposed group of more than 1,000 lifetime working hours included 18.6% of cases and 10% of controls. Without adjustment, the OR for asbestos exposure was 2.1, but after adjustment for tobacco and alcohol, it decreased to 1.3 (95% CI: 0.8–2.1), which was not significant. Thus, we present results without adjustment for asbestos in our analyses.

Eligible for the validation study with the mentioned cement-specific questionnaire were 58 cement dust exposed cases and 106 controls. The cement specific interviews were arranged 2–4 years after the first interview in the clinics. Only 28 cases and 99 controls could be reached for further assessment because of death, loss of contact, etc, and 15 cases and 80 controls accepted a telephone interview to conduct the cement-specific questionnaire.

All 15 cases (100%) classified as exposed in our main study also reported an exposure in the re-interview. However, in controls, only 69/80 (86.3%) confirmed cement dust exposure. Although this difference in proportions is not significant ($p = 0.16$, Fisher exact test), it indicates that exposure to cement in the control group is more likely to have been overestimated than in controls in the original interview. This means that the reported ORs may be underestimated, which emphasizes the assessment of cement dust exposure as relevant risk factor for laryngeal cancer. Distinguishing between exposure to cement and lime or slaked lime, 9/15 (60.0%) of cases and 34/80 (42.5%) of controls were exposed to any kind of lime. Considering the exposure frequency of lime in cases and controls, we observed that a higher percentage of cement-exposed cases also had a lime exposure (60%) compared to controls (48.6%). This indicates that lime exposure may have an additional harmful effect. The data allow an estimation of the OR for lime exposure given cement exposure, yielding an OR of 2.0 (not significant). If high exposure (> 3,000 hr) is considered, the OR is 3.6 (95% CI 1.1–11.9). However numbers are too small to draw definite conclusions. (Table III).

TABLE II – CEMENT DUST EXPOSURE IN CASES AND CONTROLS AND ODDS RATIOS

Cement dust exposure	Cases				Controls				OR_1	OR_2	OR_3	95% CI	p-value
	Male		Female		Male		Female						
	n	(%)	n	(%)	n	(%)	n	(%)					
Assessed by job-specific questionnaires													
Not exposed	201	85.2	21	100.0	666	94.9	66	98.5	1	1	1		
Exposed	35	14.8			36	5.1	1	1.5	3.13*	2.39*	2.04	1.16–3.56	0.01
Assessed by list of hazardous substances													
Not exposed	181	76.7	21		601	85.6	66	98.5	1	1	1		-
Exposed	55	23.3			101	14.4	1	1.5	1.76*	1.45	1.18	0.77–1.81	0.45
Cement exposure rating													
Not exposed (0 h)	201	85.2	21	100.0	666	94.9	66	98.5	1	1	1		
(Lifetime working hours)													
Middle exposed (0–≤3000)	16	6.8			17	2.4			3.10*	2.35*	2.22	1.02–4.84	0.04
High exposed (3000+)	19	8.1			19	2.7			3.17*	2.42*	1.87	0.88–4.01	0.11
Sum	236	100.0	21	100.0	702	100.0	67	100.0					

OR_1, Odds Ratio, stratificed for age and gender; OR_2, Odds Ratio, stratificed for age and gender, adjusted for tobacco and alcohol intake; OR_3, Odds Ratio, stratificed for age and gender, adjusted for tobacco, alcohol intake and socioeconomic status; *, ($p < 0.05$, two side test); 95% CI, 95% confidence interval for OR_3.

TABLE III – VALIDATION STUDY WITH CEMENT SPECIFIC QUESTIONNAIRE IN A SUBGROUP (15 LARYNGEAL CANCER PATIENTS, 80 CONTROLS) OF PARTICIPANTS HAVING BEEN DOCUMENTED AS CEMENT EXPOSED IN THE FIRST INTERVIEW

Exposure to	Cases		Controls	
	n	%	*n*	%
Cement				
Any cement at work	6	40	40	50
Mixing of cement binder	8	53.3	52	65
Cement processing	7	46.7	20	25
Rating of cement exposure				
No exposure	0	–	0	–
(Life working hours)				
Middle exposure (≤=3000 hrs)	6	40	32	40
High exposure (> 3000 hrs)	9	60	38	47.5
Lime[1]				
Not slaked	1	6.7	3	3.8
Slaked	6	40	25	31.2
Slaked in person	5	33.3	10	12.5
Processing of lime plaster	5	33.3	15	18.8
Rating of lime exposure				
No exposure	6	40	46	57.5
(Life working hours)				
Middle exposure (≤ 3,000 hrs)	1	6.7	17	21.25
High exposure (> 3,000 hrs)	8	53.3	17	21.25
Using only cement	6	40	36	45
Using only lime	0	–	0	–
Using cement and lime	9	60	34	42.5
Using neither cement nor lime	0	–	10	11.5
Sum	15	100%	80	100%

[1]Multiple entries possible.

DISCUSSION

The Rhein Neckar Larynx Study, which is partly introduced in this article, is one of the largest population-based case-control studies on laryngeal cancer. One of the important findings in our study was the probability of an independent risk of cement dust for laryngeal cancer. Regarding the tobacco and alcohol adjusted OR of 2.35 in the middle exposed group (0 to ≤ 3,000 lifetime working hours) and 2.42 in the high exposed group (> 3,000 lifetime working hours, Table II), there is a slight dose-response effect. But after adjustment of socioeconomic factors (Table II: OR_3), dose response effects disappeared completely in our sample group. However, further distributions in dose-related groups are not useful due to methodologic reasons, so that validity of our data concerning dose response effects is limited.

Interestingly, the data of the validation study with cement specific questionnaire in a representative subgroup (15 laryngeal cancer patients, 80 controls) of participants (documented as cement exposed in the first interview: Table III) signified exposure to cement in the group of controls as probably overestimated in the first census. For all 15 cases (100%), cement dust exposure was verified. However, 11 (13.7%) control persons reported no cement exposure after additional assessment. Even though evidence is limited due to the small sample group of the validation study, the findings suggest that OR estimates of cement exposure may gain further significance.

An additional adjustment for asbestos exposure would be possible to exclude possible confounding. Because we did not find a relevant risk for asbestos and laryngeal cancer, OR estimates remain virtually unchanged if we nevertheless perform asbestos adjustment.

Our cement-specific post-assessment allowed us to distinguish between cement and lime; in the 50s and early 60s of the last century, direct processing of slaked lime in place of Portland cement was very common. In discussion of cement exposure, it therefore has to be considered that lime dust exposure of former times is often lumped together with cement. Especially during slaking of lime, it has to be assumed that strong formation of lime dust takes place. But none of the participants categorized as cement exposed had exclusive contact with lime. Predominant exposure to both materials (lime and cement) was indicated (60% of cases, 42.5% of controls). In the literature, exposure to lime was associated with oesophageal carcinoma.[34] In the case of many oropharyngeal and oral cavity cancers in Asia, Africa and Papua New Guinea, it is the alkaline slaked lime in the betel quid that is probably responsible; regarding gastric cancers, it is the reflux of the alkaline duodenal contents into the stomach after alimentation of betel quid.[35,36] But cancer of the head and neck region associated with lime or slaked lime in builders dust has not been described so far.

One of the most meaningful dues of builder's dust is cement (combined with slaked lime in former years), which might be responsible for elevated carcinoma risk of the larynx, and brings up the question of what the cancer boosting agent in cement (lime) dust could be. Cement (in particular Portland cement, which is mostly used in Europe) is a composition of calcium oxide (62–66%), silicium oxide (19–22%), aluminum trioxide (4–8%) iron oxide (2–5%), magnesium oxide (1–2%) sulphur oxide and alkali oxides that are responsible for the properties of the adhesive agent. Also, small doses of microelements like chromium are found. Above all, chromium-VI-compounds were categorized as human carcinogen by the IARC in 1980.[37] Concentration of chromium ranges between 20–100 ppm, partly up to 200 ppm, which allows the expression microelement. The main origin of chromium in cement is clay and lime. Chromium is changed to chromium (VI) after combustion of basic materials. Soluble chromium (VI) is well known as a trigger for allergic cement dermatitis, which is also promoted by the alkali and irritating milieu of water diluted processed cement. Chromium (VI) penetrates the skin more easily than other chromium compounds, like chromium (III). This affected the development of chromium reduced grades of cement in the last decades, due to iron-(II)-sulphate for instance.[38] Beside chromium, other microelements like nickel, zinc, lead, titanium, cadmium and arsenic are present in cement dust. These elements do not affect the consistency of cement but their concentration varies because fluctuations in the raw material are described (e.g., arch ledge in stone deposit) and there is increasing combustion of rubber wheel or oil residues in cement fabrication.[39] Whether the small dose of chromium (VI) or other elements like arsenic in cement dust are really able to cause cancer of the laryngeal mucous membranes is not yet clear.

Another explanation for the relationship of laryngeal cancer and cement dust exposure could be the strong cement associated alkali reaction. The particles in cement dust ranges between 0.01–200 μm, predominantly between 1 and 50 μm (the fraction of particles smaller than 8 μm is estimated to be 30–50%). Accordingly, sedimentation of inhaled cement dust takes place in the upper and lower aerodigestive tract, particularly in the larynx. After getting wet, it is likely that cement dust causes a strong basic reaction that leads to increased pH-values (12.5–13.0) on the touched mucous membranes of the larynx. This could be a feasible explanation of the advanced susceptibility to several carcinogens like tobacco, PAHs, etc.

In conclusion, our data on exposure to cement dust—merging slaked lime before about 1965 and Portland cement afterwards—shows a tobacco, alcohol and socioeconomic independent, statistically significant elevated risk for laryngeal carcinoma. This risk is also autonomous regarding asbestos and other described risk factors. The Rhein-Neckar-Larynx Study affirmed observations of former studies and singles out cement dust exposure as a more serious candidate for further toxicologic investigations focusing on the development of laryngeal cancer.

ACKNOWLEDGEMENTS

We acknowledge the contribution of Dr. M.-L. Groβ who organised the interviews of patients and controls. Our study would not have been possible without the cooperation of clinicians from the following clinics: Universität HNO-Klinik Heidelberg (Prof. Dr. H. Weidauer), Universität HNO-Klinik Mannheim (Prof. Dr. K. Hörmann), HNO-Klinik der Städt. Kliniken Darmstadt, (Prof. Dr. K. Reck), HNO-Klinik der Städt. Kliniken Ludwigshafen (Prof. Dr. G. Münker [deceased], PD Dr. K.-W. Delank) and HNO-Klinik der Städt. Krankenanstalten Heilbronn (Prof. Dr. C. Naumann). Additionally, we thank Prof. Dr. H. Maier, HNO-Abteilung BWK Ulm, for helpful assistance in preparation of the proposal for our study.

REFERENCES

1. Eckel H, Stennert E. Kopf-Hals-Karzinome, Spezielle Diagnostik und Therapie. In: Zeller – zur Hausen, Onkologie, 3.Erg.Lfg.5/97, Kap. V2.4. 1997.
2. Cattaruzza MS, Maisonneuve P, Boyle P. Epidemiology of laryngeal cancer. Oral Oncol Eur J Cancer 1996;32B,5:293–305.
3. Jöckel KH, Ahrens W, Jahn I, Pohlabeln H, Bolm-Audorff U. Occupational risk factors for lung cancer: a case-control study in West Germany. Int J Epidemiol 1998;24:549–60.
4. Landrigan PJ, Markowitz S. Current magnitude of occupational diseases in the United States: estimates from New York State. Ann NY Acad Sci 1989;572:27–45.
5. Chang-Claude J. Larynxkarzinom durch Asbest? - ein Bericht aus epidemiologischer Sicht. BK-Report Larynxkarzinom durch Asbest? Schriftenreihe des Hauptverbandes der gewerblichen Berufsgenossenschaften, Sankt Augustin 1994.
6. Ahrens W, Jockel KH, Patzak W, Elsner G. Alcohol, smoking, and occupational factors in cancer of the larynx: a case-control study. Am J Ind Med 1991;20:477–93.
7. Morris-Brown L, Mason TJ, Williams-Pickle L, Stewart PA, Buffler PA, Ziegler RG, Fraumeni JF. Occupational risk factors for laryngeal cancer on the Texas Gulf Coast. Cancer Res 1988;48:1960–4.
8. Muscat JE, Wynder EL. Tobacco, alcohol, asbestos, and occupational risk factors for laryngeal cancer. Cancer 1992;69:2244–51.
9. Dietz A, Sennewald E, Maier H. Indoor air pollution by emissions of fossil fuel-single stoves—possibly a hitherto underrated risk factor in the development of carcinomas in head and neck. Otolaryngol Head Neck Surg 1995;2:308–15.
10. Gustavsson P, Jakobsson R, Johansson H, Lewin F, Norell S, Rutkvist LE. Occupational exposures and squamous cell carcinoma of the oral cavity, pharynx, larynx, and oesophagus: a case-control study in Sweden. Occup Environ Med 1998;55:393–400.
11. Maier H, Sennewald E. Risikofaktoren für Plattenepithelkarzinome im Kopf-Hals-Bereich - Ergebnisse der Heidelberger Fallkontrollstudien. Hauptverband der gewerblichen Berufsgenossenschaften (HVBG) Januar. 1994.
12. Pollan M, Lopez-Abente G. Wood-related occupations and laryngeal cancer. Cancer Detect Prev 1995;19:250–7.
13. Schwartz E. A proportionate mortality ratio analysis of pulp and paper, ill workers in New Hampshire. Br J Ind Med 1988;45:234–8.
14. Kennaway NM, Kennaway EL. A study of the incidence of cancer of the lung and larynx. J Hygiene 1936;36:236–67.
15. Elci OC, Dosemeci M, Blair A. Occupation and the risk of laryngeal cancer in Turkey. Scand J Work Environ Health 2001;27:233–9.
16. Decoufle P. Cancer risks associated with employment in the leather and leather products industry. Arch Environ Health 1979;34:33–37.
17. Tisch M, Munch P, Maier H. Do employees in the rubber industry have an increased risk of laryngeal cancer? HNO 1995;43:649–53.
18. IARC. IARC monographs programme on the evaluation of carcinogenic risks to humans. Supplement No. 7: overall evaluations of carcinogenicity. An updating of IARC monographs 1987; Vol. 1–42.
19. Maier H, Tisch M. Epidemiology of laryngeal cancer: results of the Heidelberg Case-Control Study. Acta Otolaryngol 1997;527:160–4.
20. Flanders WD, Rothman KJ. Occupational risk for laryngeal cancer. Am J Public Health 1982;72:369–72.
21. Wortley P, Vaughan TL, Davis S, Morgan MS, Thomas DB. A case-control study of occupational risk factors for laryngeal cancer. Br J Ind Med 1992;49:837–44.
22. Olsen J, Sabroe S. Occupational causes for laryngeal cancer. J Epidemiol Community Health 1984;38:117–21.
23. Robinson C, Stern F, Halperin W. Assessment of mortality in the construction industry in the United States 1984–86. Am J Ind Med 1995;28:49–70.
24. Maier H, Gewelke U, Dietz A, Heller WD. Risk factors of cancer of the larynx: results of the Heidelberg case-control study. Otolaryngol Head Neck Surg 1992;197:577–82.
25. Cauvin JM, Guenel P, Luce D, Brugere J, Leclerc A. Occupational exposure and head and neck carcinoma. Clin Otolaryngol 1990;15: 439–45.
26. Jakobsson K, Attewell R, Hultgren B, Sjöland K. Gastrointestinal cancer among cement workers. A case–referent study. Int Arch Occup Environ Health 1990;62:337–40.
27. Ramroth H, Altenburg HP, Becher H. Auswahl von Populationskontrollen für epidemiologische Fall-Kontroll-Studien unter Verwendung regionaler Stichproben. Informatik, Biometrie und Epidemiologie in Medizin und Biologie 2001;32:60–70.
28. Ahrens W, Jöckel K, Brochard P, Bolm-Audorff U, Grossgarten K, Iwatsubo Y, Orlowski E, Pohlabeln H, Berrino F. Retrospective assessment of asbestos exposure. I. Case-control analysis in a study of lung cancer: efficiency of job-specific questionnaires and job exposure matrices. Int J Epidemiol 1993;22(Suppl 2):83–95.
29. Ahrens W, Jöckel K-H, Pohlabeln H, Bolm-Audorff U, Iwatsubo Y, Brochard P, Berrino F, Orlowski E. Assessment of exposure to asbestos in a case-control study of lung cancer: comparison of supplementary questionnaires and an exposure check-list. Occup Hyg 1996; 3:125–36.
30. Metzler-Poeschel. Klassifikation der Wirtschaftszweige mit Erläuterungen. Statistisches Bundesamt, W. (ed.). NACE Rev. 1, Council Regulation [EEC] No. 3037/90 [O.J. L 293 of 24.10.1990] as modified by Council Regulation [EEC] No. 761/93 [O.J. L 83 of 3.4.1993], EUROSTAT Unit B6. Stuttgart 1993.
31. International Labour Organisation (ILO). International standard classification of occupations (ISCO), 2nd ed. Geneva: ILO Publications, 1968.
32. Jöckel K-H, Ahrens W, Wichmann H-E, Becher H, Bolm-Audorff U, Jahn I, Molik B, Greiser E, Timm J. Occupational and environmental hazards associated with lung cancer. Int J Epidemiol 1992;21:202–13.
33. Neuhäuser M, Becher H. Improved odds ratio estimation by post-hoc stratification of case-control data. Stat Med 1997;16:993–1004.
34. Ghavamzadeh A, Moussavi A, Jahani M, Rastegarpanah M, Iravani M. Esophageal cancer in Iran. Semin Oncol 2001;28:153–7.
35. Thomas SJ, MacLennan R. Slaked lime and betel nut cancer in Papua New Guinea. Lancet 1992;340:577–8.
36. Malhotra SL. New approaches to the causation and prevention of cancers of epithelial surfaces. Med Hypotheses 1976;2:279–81.
37. IARC. Monographs on the evaluation of the carcinogenic risk of chemicals to humans 1980;23:205–32.
38. Die Bedeutung des Chromats in Zementen und zementhaltigen Zubereitungen; Sachstandsbericht, Fassung 05.01.99, Forschungsinstitut der Zementindustrie, Verein deutscher Zementwerke e.V 1999.
39. Lawrence DD. The constitution and specification of Portland. In: Hewlett PC, ed. Lea's chemistry of cement and concrete. London: Arnold, 1998. 131–91.

EXHIBIT 8

Int. J. Cancer: **120,** 2013–2018 (2007)

Airborne exposures and risk of gastric cancer: A prospective cohort study

Krister Sjödahl[1]*, Catarina Jansson[1], Ingvar A. Bergdahl[2], Johanna Adami[2,3], Paolo Boffetta[2,4] and Jesper Lagergren[1]

[1]*Unit of Esophageal and Gastric Research (ESOGAR), Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden*
[2]*Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden*
[3]*Clinical Epidemiology Unit, Department of Medicine, Karolinska University Hospital, Stockholm, Sweden*
[4]*International Agency for Research on Cancer, Lyon, France*

There is an unexplained male predominance among patients with gastric cancer, and many carcinogens are found in male-dominated dusty occupations. However, the relation between occupational exposures and risk of gastric cancer remains unclear. To investigate whether airborne occupational exposures might influence the risk of noncardia gastric cancer, we used a large, prospective cohort study of male Swedish construction workers. These workers were, during the period 1971–1993, regularly invited to health examinations by a nationwide occupational health service organization. Data on job titles and other variables were collected through self-administered questionnaires and forms completed by the health organization's staff. Industrial hygienists assessed 12 specific airborne occupational exposures for 200 job titles. Gastric cancer, death or emigration occurring during follow-up in 1971–2002 were identified by linkage to the Swedish registers of Cancer, Causes of Death and Total Population, respectively. Incidence rate ratios (IRR) and 95% confidence intervals (CI), adjusted for attained age, tobacco smoking, calendar period and body mass, were derived from Cox regression. Among 256,357 cohort members, contributing 5,378,012 person-years at risk, 948 noncardia gastric cancers were identified. Increased risk of this tumor was found among workers exposed to cement dust (IRR 1.5 [95% CI 1.1–2.1]), quartz dust (IRR 1.3 [95% CI 1.0–1.7]) and diesel exhaust (IRR 1.4 [95% CI 1.1–1.9]). Dose-response relations were observed for these exposures. No consistent positive associations were found regarding exposure to asbestos, asphalt fumes, concrete dust, epoxy resins, isocyanates, metal fumes, mineral fibers, organic solvents or wood dust. In conclusion, this study provides some support to the hypothesis that specific airborne exposures increase the risk of noncardia gastric cancer.

Key words: neoplasm; adenocarcinoma; stomach; environmental; risk factor

Despite the declining incidence of noncardia gastric cancer in developed countries during the past decades,[1,2] this malignancy remains a major health concern globally, as it is the fourth most common cancer and the second leading cause of cancer-related death worldwide.[3] Advances in diagnostic and therapeutic procedures have not had much influence on the poor prognosis for gastric cancer patients,[3] stressing the urgent need for research that can identify preventable risk factors. Infection with the bacteria *Helicobacter pylori* (*H. pylori*) is a main known causative agent of noncardia gastric cancer.[4,5] Moreover, tobacco smoking[6] and low socioeconomic status[2] have consistently been associated with moderately increased risks, and some dietary factors have also been linked with this cancer.[7,8] The recent etiologic research on gastric cancer has focused on *H. pylori*, but this infection is difficult to prevent or broadly eradicate, and it cannot explain the male predominance of patients with gastric cancer (2–3 to 1).[2] Thus, yet unidentified environmental risk factors might be of relevance. In many male-dominated industries, the exposure to carcinogenic agents is high, and the reduction of occupational chemical hazards in industrialized countries during recent decades[9] seems to have coincided with the falling incidence of gastric cancer, indicating a possible etiologic role of occupational exposures. In line with this, several occupations and "dusty" work environments have been implicated in the etiology of this disease,[10–12] but unfortunately, the scientific evidence regarding an association between dust exposure and risk of gastric cancer is insufficient and there is a need for further investigations of specific agents.[10] We hypothesized that specific airborne exposures, which often occur in the construction industry, such as dust, fumes and solvents, could be inhaled and swallowed and have a direct harmful effect on the gastric mucosa. With the aim of clarifying the relation between such exposures and risk of gastric cancer in a male-dominated industry, we used prospectively collected data for a large cohort of Swedish construction workers.[13]

Methods

Study design

Diverging incidence trends, marked geographic variation and different risk factor profiles indicate that gastric cardia and noncardia cancer represent separate disease entities.[2] The present study was therefore restricted to noncardia gastric cancer. Hence, when we use the term gastric cancer in the following, cardia cancer cases are excluded. The methods used has been presented in detail in our study addressing airborne occupational exposures and risk of esophageal and gastric cardia cancer.[14] In brief, the Swedish Construction Workers Cohort consists of almost 400,000 employees within the Swedish construction industry who between 1971 and 1993 were regularly invited to attend health examinations by a nationwide occupational health service organization with almost complete coverage of the construction industry.[13] The participation rate among the invited persons was high (85–90%). Information on job titles and other variables, notably tobacco smoking and anthropometric measures, was obtained prospectively through self-administered questionnaires and forms completed by specially trained nurses within the health service organization. Since 95% of the cohort members were men, no women were included in the current study. The National Registration Number, a unique personal identifier assigned to all Swedish residents, was used to identify each cohort member and to link each member to the nationwide Swedish Cancer Register. By this means, all incident cases of gastric cancer occurring during follow-up of the cohort, in 1971 through 2002, were identified. The Swedish Cancer Register codes gastric tumors (ICD-7: 1510, 1518 and 1519) with an overall completeness of 98%.[15,16] For complete follow-up and for correct censoring of persons in whom death or emigration precluded the risk of gastric cancer, each cohort member was also linked to the nationwide Swedish registers of Causes of Death and the Total Population.

Grant sponsor: Swedish Cancer Society.
***Correspondence to:** Unit of Esophageal and Gastric Research, P9:03, Department of Molecular Medicine and Surgery, Karolinska Institutet, SE-171 76 Stockholm, Sweden. Fax: +46-8-33-15-87.
E-mail: krister.sjodahl@ki.se
Received 13 September 2006; Accepted after revision 28 November 2006
DOI 10.1002/ijc.22566
Published online 31 January 2007 in Wiley InterScience (www.interscience.wiley.com).

TABLE I – NO. OF PARTICIPANTS, PERSON-YEARS AND INCIDENCE RATES (IR) OF NONCARDIA GASTRIC CANCER BY ATTAINED AGE, CALENDAR PERIOD, TOBACCO SMOKING STATUS AND BODY MASS INDEX

Characteristic	No. of subjects, N(%)	Person-years	Gastric Cancer	
			All cases	IR[1]
Attainted age, yr				
≤34	154,108	1,487,583	4	0.3
35–39	154,481	638,794	5	0.8
40–44	142,361	592,700	21	3.5
45–49	132,575	566,918	29	5.1
50–54	127,207	533,348	46	8.6
55–59	114,781	458,478	88	19.2
60–64	93,383	382,474	142	37.1
65–69	70,867	301,320	171	56.8
70–74	50,961	210,080	196	93.3
75–79	33,222	127,013	141	111.0
80–84	17,995	59,022	69	116.9
≥85	6,709	20,282	36	177.5
Calendar period at entry into the cohort				
1971–75	121,441 (47)	3,157,709	842	26.7
1976–80	23,902 (9)	531,385	45	8.5
1981–93	111,014 (43)	1,688,918	61	3.6
Tobacco smoking status at entry into the cohort				
Never	111,459 (43)	2,165,694	253	11.7
Previous	41,197 (16)	943,801	238	25.2
Current	103,701 (40)	2,268,516	457	20.2
Body mass index[2] at entry into the cohort				
≤21.9 low weight	65,962 (26)	1,387,301	174	12.5
22.0–24.9 normal weight	100,734 (39)	2,133,156	358	16.8
25.0–29.9 overweight	77,857 (30)	1,627,372	361	22.2
≥30.0 obese	11,804 (5)	230,183	55	23.9
Total[3]	256,357	5,378,012	948	17.6

[1]Incidence rates per 100,000 person-years.–[2]BMI (body mass index) calculated as body weight in kilograms divided by the square of body height in meters (kg/m^2).–[3]Observations with missing data for any characteristic included in this table were excluded from the analyses.

Assessment of airborne occupational exposures

The exposure assessment was based on job titles as described in previous reports.[13,14,17,18] Only the job title at each worker's first health examination was used, as we lacked information for constructing lifetime occupational histories. Between 1971 and 1976, industrial hygienists assessed the exposure patterns within more than 200 occupations specific for the Swedish construction industry. Each of these occupations was studied at visits to ~5 different sites in different geographical regions in Sweden. The job-exposure matrix regarding airborne exposures included 12 agents: asbestos, asphalt fumes, cement dust, concrete dust, diesel exhaust, epoxy resins, isocyanates, mineral fibers, metal fumes, organic solvents, quartz dust and wood dust. Each of these exposures was graded on an ordinal scale from 0 to 5, where level 3 corresponded to the Swedish threshold limit value at the time of the study. When no such limits were applicable, level 3 corresponded to an exposure level considered to be "acceptable" at that time. No specific quantitative meaning was assigned to the other grades. The exposure level scales were categorized into no exposure (0), moderate exposure (0.5–1) and high exposure (2–5). We also examined exposure to "combined" dust (defined as exposure to any of the following: asbestos, cement dust, concrete dust, mineral fibers, quartz dust or wood dust) and fumes (defined as diesel exhaust, asphalt fumes or metal fumes).

Statistical analyses

The cohort members were followed up from the date of their first health examination through December 31, 2002, the date of death, date of emigration or date of a primary gastric cancer diagnosis, whichever occurred first. Cox regression[19] was used to estimate incidence rate ratios (IRR) and 95% confidence intervals (CI), using time since entry into the cohort as the underlying timescale. Models were estimated using the PHREG procedure in SAS.[20] In multivariable models, adjustments were made for attained age (classified into 5-year age groups), calendar period at entry into the cohort (in 3 categories: 1971–1975, 1976–1980 and 1981–1993), tobacco smoking status at entry (in 3 categories: never, previous and current) and body mass index (BMI) at entry (in 4 categories: ≤21.9 [low], 22.0–24.9 [normal], 25.0–29.9 [overweight] and ≥30 [obese]). Individuals with missing data for any of the covariates included in the models were excluded from the analyses. The overall effect of each covariate was assessed by a Wald test of homogeneity across all exposure strata.

Results

Study participants and incidence rates of gastric cancer

From the original cohort of 384,147 members, we excluded all women (n = 19,224) and men with (*i*) a diagnosis of gastric cancer before their first visit (n = 31), (*ii*) incorrect death dates (n = 28) or (*iii*) missing or insufficient information on job title, smoking status (mainly due to lack of recording of smoking status during 1975–1978) and/or BMI (n = 108,507). Hence, 256,357 men constituted the final study cohort. Together, these study participants contributed 5,378,012 persons-years at risk of developing gastric cancer during the follow-up period. In total, 948 incident cases of gastric cancer were identified. Some characteristics of the study participants are presented in Table I. The total incidence rate (IR) of gastric cancer was 17.6 per 100,000 person-years. The IR of gastric cancer was higher for participants who attended for their first health examination during the earliest years of inclusion into the cohort. The IR was increased among previous or current smokers, and among those who had a BMI above 25 at entry into the cohort.

Airborne occupational exposures and risk of gastric cancer

The relative risk estimates based on the adjusted models are presented in Table II. There were positive associations, seemingly with dose-response relationships between exposure to cement

TABLE II – NO. OF PARTICIPANTS, PERSON-YEARS AND INCIDENCE RATE RATIOS (IRR) FOR NONCARDIA GASTRIC CANCER ASSOCIATED WITH OCCUPATIONAL EXPOSURES AMONG SWEDISH CONSTRUCTION WORKERS

Occupational exposure	No. of subjects n(%)	Person-years	Gastric cancer		
			All cases	IRR[1] (95% CI)	p value[2]
Asbestos					
No exposure	245,872 (96)	5,134,108	920	1.0 (reference)	
Moderate exposure	6,971 (3)	160,794	21	0.8 (0.5–1.2)	
High exposure	3,514 (1)	83,111	7	0.7 (0.3–1.4)	0.33
Asphalt fumes					
No exposure	251,626 (98)	5,276,100	934	1.0 (reference)	
Moderate exposure	–	–			
High exposure	4,731 (2)	101,912	14	0.9 (0.5–1.5)	0.64
Cement dust					
No exposure	234,419 (91)	4,927,675	812	1.0 (reference)	
Moderate exposure	18,550 (7)	374,195	99	1.1 (0.9–1.4)	
High exposure	3,388 (1)	76,142	37	1.5 (1.1–2.1)	0.03
Concrete dust					
No exposure	159,661 (62)	3,340,495	586	1.0 (reference)	
Moderate exposure	48,065 (19)	969, 562	154	1.0 (0.8–1.1)	
High exposure	48,631 (19)	1,067,955	208	0.9 (0.8–1.1)	0.74
Diesel exhaust					
No exposure	222,720 (87)	4,660,435	758	1.0 (reference)	
Moderate exposure	27,889 (11)	591,487	146	1.3 (1.1–1.6)	
High exposure	5,748 (2)	126,089	44	1.4 (1.1–1.9)	<0.01
Epoxy resins					
No exposure	254,000 (99)	5,328,298	939	1.0 (reference)	
Moderate exposure	2,357 (1)	49,714	9	0.7 (0.4–1.4)	0.30
High exposure	–	–			
Isocyanates					
No exposure	240,068 (94)	5,088,919	903	1.0 (reference)	
Moderate exposure	15,431 (6)	271,963	41	1.2 (0.8–1.6)	
High exposure	858 (<1)	17,131	4	1.6 (0.6–4.2)	0.46
Metal fumes					
No exposure	232,107 (91)	4,863,320	867	1.0 (reference)	
Moderate exposure	1,092 (<1)	19,738	3	0.7 (0.2–2.2)	
High exposure	23,158 (9)	494,955	78	1.0 (0.8–1.3)	0.83
Mineral fibers					
No exposure	237,113 (92)	4,965,554	887	1.0 (reference)	
Moderate exposure	12,122 (5)	261,002	50	1.1 (0.9–1.5)	
High exposure	7,122 (3)	151,457	11	0.6 (0.3–1.0)	0.12
Quartz dust					
No exposure	205,286 (80)	4,277,595	690	1.0 (reference)	
Moderate exposure	42,165 (16)	904,552	200	1.2 (1.0–1.4)	
High exposure	8,906 (3)	195,865	58	1.3 (1.0–1.7)	0.03
Organic solvents					
No exposure	228,915 (89)	4,804,594	885	1.0 (reference)	
Moderate exposure	7,014 (3)	150,690	18	0.7 (0.4–1.1)	
High exposure	20,428 (8)	422,728	45	0.6 (0.5–0.9)	<0.01
Wood dust					
No exposure	239,004 (93)	5,030,241	892	1.0 (reference)	
Moderate exposure	16,796 (7)	334,135	53	0.9 (0.7–1.2)	
High exposure	557 (<1)	13,636	3	1.2 (0.4–3.6)	0.65
Dust[3]					
Unexposed	114,226 (45)	2,374,208	367	1.0 (reference)	
Exposed	142,131 (55)	3,003,804	581	1.0 (0.9–1.3)	0.59
Fumes[4]					
Unexposed	199,250 (78)	4,161,867	686	1.0 (reference)	
Exposed	57,107 (22)	1,216,145	262	1.2 (1.1–1.4)	<0.01
Total[5]	256,357	5,378,012	948		

[1]In the multivariable Cox regression models adjustments were made for attained age (in 5-year age-groups), calendar period at entry into cohort (in 3 categories; 1971–75, 1976–80, 1981–93), tobacco smoking at entry into cohort (in 3 categories; never, previous and current), and BMI at entry into cohort (in 3 categories: ≤21.9 underweight, 22.0–24.9 normal, 25.0–29.9 overweight and ≥30.0 obese).–[2]Wald test of overall effect across all occupational exposure strata.–[3]Combined dust exposure, defined as exposure to: asbestos. cement dust, concrete dust, mineral fibers, quartz dust, of wood dust.–[4]Combined exposure to fumes defined as of exposure to asphalt fumes, diesel exhaust or metal fumes.–[5]Observations with missing data for any covariate included in the models were excluded from the analyses.

dust, quartz dust and diesel exhaust and risk of gastric cancer. Statistically, significantly increased risks of gastric cancer were found among workers highly exposed to cement dust (IRR 1.5 [95% CI 1.1–2.1]), quartz dust (IRR 1.3 [95% CI 1.0–1.7]), diesel exhaust (IRR 1.4 [95% CI 1.1–1.9]) and among workers exposed to "combined" fumes (IRR 1.2 [95% CI 1.1–1.4]). A negative association was observed between exposure to organic solvents and risk of gastric cancer (IRR 0.6 [95% CI 0.5–0.9]). No consistent associations were found between exposure to any of the other studied specific agents or "combined" dust exposure and risk of gastric cancer (Table II).

Discussion

This study indicates positive, dose-dependent associations between exposure to cement dust, quartz dust and diesel exhaust and risk of gastric cancer. No such increased risk was detected among workers exposed to asbestos, asphalt fumes, concrete dust, epoxy

resins, isocyanates, mineral fibers, metal fumes, organic solvents or wood dust.

Strengths and limitations of the study methods deserve some attention. The statistical power is good, by virtue of the large number of participants, recruited through an organization with almost complete coverage of employees in the Swedish construction industry in 1971 through 1993.[13] Other advantages include the prospectively collected information regarding job titles and the unbiased expert exposure assessment, the long and complete follow-up, and the availability of information on potential confounding by tobacco smoking and other variables. Moreover, each individual's job title was linked to a job-exposure matrix developed by industrial hygienists, and thus specific agents could be analyzed. However, this type of job-exposure matrices has some limitations,[21] *e.g.* possible exposure misclassification. We were unable to study lifetime occupational histories, *i.e.* duration of exposure, and could only use the job title at the first visit as information regarding previous occupations was insufficient before 1986 and not collected after 1986. Moreover, the exposures were based solely on job titles, and not on each individual's unique exposure. However, in a previous study based on this cohort, it was found that among workers examined before 1986 few persons had changed their work tasks, and 96.3% had the same exposure level for both previous and current job title, indicating that the construction industry has a stable work force.[22] Moreover, the job-exposure matrix was based on detailed expert assessments of exposure patterns. Another potential weakness is a lack of data concerning some potential confounders, including *H. pylori* infection. But any association between the studied exposures and *H. pylori* infection in this cohort is not likely to be strong enough to cause appreciable confounding, if any. Moreover, the high socioeconomic homogeneity of the cohort reduces potential confounding associated with such infection or with lifestyle factors. Finally, any "healthy worker effect" was avoided, since workers were internally compared.[23]

There have been reports on positive associations between various occupational groups and risk of gastric cancer,[10,12] notably "dusty" occupations, *e.g.*, coal and tin mining,[24–29] metal processing,[30–35] rubber manufacturing[36–40] and carpentry or construction work.[10,12] Other dusty work environments have also been implicated in the etiology.[41–44] However, possible occupational exposures linked to a risk of gastric cancer have not been established, since the majority of previous studies have not addressed specific exposures, have not adjusted for potential confounders, or have revealed only weak associations without dose-response patterns.[10]

Our finding of an increased risk of gastric cancer among workers exposed to cement dust is interesting. However, the highly exposed persons in our cohort mainly consisted of storage-workers who may be generally less fit than other workers, which would mean that confounding cannot be ruled out. These storage-workers were often handling "fresh" cement, carrying on their backs large sacks of it (unpublished information). Therefore, it is likely that the most highly cement exposed workers in this cohort have been exposed to fresh cement in warehouses, and not to concrete-related cement. Our results are supported by a study of Lithuanian cement masons,[45] and a study of US cement-producing workers,[46] while no clear associations were found in other studies of cement workers in Sweden or the US.[47,48] The positive association between quartz dust and risk of gastric cancer found in our study is in line with reports on workers exposed to silica dust in Canada,[49–51] Spain[28] and Japan.[52] The current large and prospective cohort study design that revealed positive, dose-response associations regarding both cement dust and quartz dust provides valid support in favor of true relations between these exposures and gastric cancer.

Diesel exhaust contains several carcinogenic chemicals, such as polycyclic aromatic hydrocarbons.[18] Increased risks of gastric cancer have been found in studies of lorry drivers in London[53] and professional drivers in Geneva.[54] Our study adds some evidence of a true link between diesel exhaust and the risk of gastric cancer.

Asbestos is a well-known human carcinogen, causing for example pleural mesothelioma and lung cancer,[9] but with regard to gastric cancer previous reports have been contradictory. In a recent Norwegian study, a possibly increased risk of gastric cancer was found among lighthouse keepers who drank water highly contaminated with asbestos,[55] and similar weak positive associations with gastric cancer have been reported from other studies of workers exposed to asbestos.[56–60] In other investigations, however, no such association has been found.[35,61–63] The lack of association between exposure to asbestos and risk of gastric cancer in our study further argues against influence of airborne asbestos in the etiology of gastric cancer.

In an earlier follow-up of this cohort studying only concrete workers, and not specific exposures, a significantly increased risk of gastric cancer was detected compared to the general Swedish population (SIR 1.39 [95% CI 1.22–1.58]).[64] Our study did not confirm these findings, however. Concrete workers are to some extent also exposed to cement dust and quartz dust, and the positive finding in the previous study might be explained by exposure to cement dust or quartz dust, and not concrete dust.

In some previous studies, positive associations have been found between metal-related work and risk of gastric cancer.[10] One Swedish study showed an excess risk of gastric cancer among metal industry workers that seemed to increase with longer duration of employment.[35] Exposure to metal fumes is low in the construction industry as compared to the metal industry, and no association between exposure to metal fumes and risk of gastric cancer was detected in our study.

Painters form the dominating occupational group exposed to organic solvents, and in a previous investigation the risk of gastric cancer by occupational groups in Sweden 1971–1989, a decreased risk was detected among painters.[12] This is in line with the results of the current study. However, no association between specific exposure to organic solvents and risk of gastric cancer was found in a Swedish case-control study.[35] Furthermore, a negative association between exposure to organic solvents and risk of gastric cancer might not be biologically plausible, and the finding might be due to chance. Alternatively, this decreased risk may reflect a possibility that workers heavily exposed to organic solvents are less likely to be exposed to other risk factors.

We hypothesized that a mechanism by which airborne particles might increase the risk of gastric cancer could be that inhaled dust and fume particles are swallowed and thereby act directly as carcinogens on the gastric mucosa. Particular agents such as cement dust and quartz dust could have an abrasive effect on the gastric mucosa, thus acting as irritants.[11,41] An inflammatory milieu can promote mitogenesis and lead to increased mutagenesis.[10,65] It is believed that excessive and continual formation of reactive oxygen species from inflammatory cells play a key role in the primary and secondary genotoxicity of fibrous and nonfibrous particles.[66] Furthermore, harmful occupational exposures most likely interact with numerous nonoccupational risk factors at various stages of gastric cancer development. Studies have shown a close linkage between low acid output and an increased concentration of nitrate and N-nitroso compounds in gastric juice.[67] In addition to its potentially abrasive effect on the gastric mucosa, a possible effect of swallowed cement dust, which is composed of chalk and clay, may be an increase in the intragastric pH. It has further been argued that dusts and fumes could potentially also act as carriers delivering other carcinogens to the stomach.[11,66] The findings in our study are not likely to be explained by such a mechanism; however, since not all of the studied particles were associated with an increased risk of gastric cancer. Indeed, our results suggest that the increased risk depends on exposure to specific types of dust particles rather than to dusty environments in general.

Although the overall burden of cancer caused by occupational exposures is probably limited,[9] involuntary exposures encountered in the working environment could have a substantial impact on the cancer risk in specific subgroups of the population, mainly

blue-collar workers. But the limited strength of the associations found in this study and the low exposure prevalence in the population at large indicate that these exposures should not materially influence the overall incidence of gastric cancer or explain the male predominance. Nevertheless, many occupational factors with an adverse effect on human health have been successfully controlled in industrialized countries, and future preventive measures should continue to target modifiable risk factors, including airborne potentially carcinogenic occupational exposures.

In conclusion, this large, prospective cohort study provides some support to the hypothesis that quartz dust, cement dust and diesel exhaust are moderate risk factors for gastric cancer. However, the studied exposures should not substantially influence the overall IR or the sex difference of this cancer, even if these associations are indeed causal. Nevertheless, preventive measures might reduce the mortality from gastric cancer among workers in highly exposed occupations.

Acknowledgements

We are grateful to all persons who designed and organized the "Bygghälsan" program, in particular Drs. Anders Englund and Göran Engholm. We thank Jenny Carlsson for administration and organization of the database.

References

1. Devesa SS, Blot WJ, Fraumeni JF, Jr. Changing patterns in the incidence of esophageal and gastric carcinoma in the United States. Cancer 1998;83:2049–53.
2. Crew KD, Neugut AI. Epidemiology of gastric cancer. World J Gastroenterol 2006;12:354–62.
3. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin 2005;55:74–108.
4. The EUROGAST Study Group. An international association between *Helicobacter pylori* infection and gastric cancer. Lancet 1993;341: 1359–62.
5. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Schistosomes, liver flukes and *Helicobacter pylori*. IARC Monogr Eval Carcinog Risks Hum 1994;61:1–241.
6. IARC. Tobacco smoking and tobacco smoke. In: IARC monographs on evaluation of carcinogenic risks to humans, vol. 83. Lyon, France: International Agency for Research on Cancer, 2002.
7. Kono S, Hirohata T. Nutrition and stomach cancer. Cancer Causes Control 1996;7:41–55.
8. WCRF&AICR. Food, nutrition and prevention of cancer: a global perspective. Washington, DC: American Institute for Cancer Research, 1997.
9. Boffetta P. Epidemiology of environmental and occupational cancer. Oncogene 2004;23:6392–403.
10. Raj A, Mayberry JF, Podas T. Occupation and gastric cancer. Postgrad Med J 2003;79:252–8.
11. Cocco P, Ward MH, Buiatti E. Occupational risk factors for gastric cancer: an overview. Epidemiol Rev 1996;18:218–34.
12. Aragones N, Pollan M, Gustavsson P. Stomach cancer and occupation in Sweden: 1971–89. Occup Environ Med 2002;59:329–37.
13. Engholm G, Englund A. Morbidity and mortality patterns in Sweden. Occup Med 1995;10:261–8.
14. Jansson C, Johansson AL, Bergdahl IA, Dickman PW, Plato N, Adami J, Boffetta P, Lagergren J. Occupational exposures and risk of esophageal and gastric cardia cancers among male Swedish construction workers. Cancer Causes Control 2005;16:755–64.
15. Mattsson B, Rutqvist LE, Wallgren A. Undernotification of diagnosed cancer cases to the Stockholm Cancer Registry. Int J Epidemiol 1985;14:64–9.
16. Ekstrom AM, Signorello LB, Hansson LE, Bergstrom R, Lindgren A, Nyren O. Evaluating gastric cancer misclassification: a potential explanation for the rise in cardia cancer incidence. J Natl Cancer Inst 1999;91:786–90.
17. Bergdahl IA, Toren K, Eriksson K, Hedlund U, Nilsson T, Flodin R, Jarvholm B. Increased mortality in COPD among construction workers exposed to inorganic dust. Eur Respir J 2004;23:402–6.
18. Lee WJ, Baris D, Jarvholm B, Silverman DT, Bergdahl IA, Blair A. Multiple myeloma and diesel and other occupational exposures in Swedish construction workers. Int J Cancer 2003;107:134–8.
19. Breslow NE, Day NE. Statistical methods in cancer research, vol. 2: The design and analysis of cohort studies. IARC Scientific Publication, 1987.
20. SAS II. Changes and enhancements through release 6.11. Cary, NC: SAS Institute, 1996.
21. Teschke K. Exposure surrogates: job-exposure matrices, self-reports, and expert evaluations. In: Nieuwenhuijsen MJ, ed. Exposure assessment in occupational and environmental epidemiology. New York: Oxford University Press, 2003.
22. Hakansson N, Floderus B, Gustavsson P, Feychting M, Hallin N. Occupational sunlight exposure and cancer incidence among Swedish construction workers. Epidemiology 2001;12:552–7.
23. Rothman K, Greenland S. Modern epidemiology, 2nd edn. Philiadelphia: Lippincott-Raven, 1998.
24. Creagan ET, Hoover RN, Fraumeni JF, Jr. Mortality from stomach cancer in coal mining regions. Arch Environ Health 1974;28:28–30.
25. Fox AJ, Goldlbatt P, Kinlen LJ. A study of the mortality of Cornish tin miners. Br J Ind Med 1981;38:378–80.
26. Stocks P. On the death rates from cancer of the stomach and respiratory diseases in 1949–53 among coal miners and other male residents in counties of England and Wales. Br J Cancer 1962;16:592–8.
27. Matolo NM, Klauber MR, Gorishek WM, Dixon JA. High incidence of gastric carcinoma in a coal mining region. Cancer 1972;29:733–7.
28. Gonzalez CA, Sanz M, Marcos G, Pita S, Brullet E, Vida F, Agudo A, Hsieh CC. Occupation and gastric cancer in Spain. Scand J Work Environ Health 1991;17:240–7.
29. Craven JL, Baum M, West RR. Variations in gastric cancer mortality in South Wales. Clin Oncol 1979;5:341–51.
30. IARC. IARC monographs for the evaluation of carcinogenic risks of chemicals to humans, vol. 83: Polynuclear aromatic compounds, Part 3: industrial exposures in aluminum production, coal gasification, coke production and iron and steel founding. Lyon, France: International Agency for Research on Cancer, 1984.
31. IARC. Overall evaluation of carcinogenicity: an updating of IARC monographs 1–42. In: IARC monographs on the evaluation of carcinogenic risks of chemicals to humans. Lyon, France: International Agency for Research on Cancer, 1987.
32. Sorahan T, Cooke MA. Cancer mortality in a cohort of United Kingdom steel foundry workers: 1946–85. Br J Ind Med 1989;46:74–81.
33. Sorahan T, Faux AM, Cooke MA. Mortality among a cohort of United Kingdom steel foundry workers with special reference to cancers of the stomach and lung, 1946–90. Occup Environ Med 1994;51:316–22.
34. Cooper WC, Wong O, Kheifets L. Mortality among employees of lead battery plants and lead-producing plants, 1947–1980. Scand J Work Environ Health 1985;11:331–45.
35. Ekstrom AM, Eriksson M, Hansson LE, Lindgren A, Signorello LB, Nyren O, Hardell L. Occupational exposures and risk of gastric cancer in a population-based case-control study. Cancer Res 1999;59:5932–7.
36. IARC. The rubber industry. In: IARC monographs for the evaluation of carcinogenic risks of chemicals to humans, vol.28. Lyon, France: International Agency for Research on Cancer, 1982.
37. Parkes HG, Veys CA, Waterhouse JA, Peters A. Cancer mortality in the British rubber industry. Br J Ind Med 1982;39:209–20.
38. McMichael AJ, Spirtas R, Kupper LL. An epidemiologic study of mortality within a cohort of rubber workers, 1964–72. J Occup Med 1974;16:458–64.
39. Monson RR, Fine LJ. Cancer mortality and morbidity among rubber workers. J Natl Cancer Inst 1978;61:1047–53.
40. Coggon D, Barker DJ, Cole RB. Stomach cancer and work in dusty industries. Br J Ind Med 1990;47:298–301.
41. Wright WE, Bernstein L, Peters JM, Garabrant DH, Mack TM. Adenocarcinoma of the stomach and exposure to occupational dust. Am J Epidemiol 1988;128:64–73.
42. Kneller RW, Gao YT, McLaughlin JK, Gao RN, Blot WJ, Liu MH, Sheng JP, Fraumeni JF, Jr. Occupational risk factors for gastric cancer in Shanghai, China. Am J Ind Med 1990;18:69–78.
43. Chow WH, McLaughlin JK, Malker HS, Weiner JA, Ericsson JL, Stone BJ, Blot WJ. Occupation and stomach cancer in a cohort of Swedish men. Am J Ind Med 1994;26:511–20.
44. Cocco P, Ward MH, Dosemeci M. Risk of stomach cancer associated with 12 workplace hazards: analysis of death certificates from 24 states of the United States with the aid of job exposure matrices. Occup Environ Med 1999;56:781–7.
45. Smailyte G, Kurtinaitis J, Andersen A. Mortality and cancer incidence among Lithuanian cement producing workers. Occup Environ Med 2004;61:529–34.
46. Stern F, Lehman E, Ruder A. Mortality among unionized construction plasterers and cement masons. Am J Ind Med 2001;39:373–88.
47. Jakobsson K, Attewell R, Hultgren B, Sjoland K. Gastrointestinal cancer among cement workers. A case-referent study. Int Arch Occup Environ Health 1990;62:337–40.

48. Amandus HE. Mortality from stomach cancer in United States cement plant and quarry workers, 1950–80. Br J Ind Med 1986;43:526–8.
49. Siemiatycki J, Gerin M, Dewar R, Lakhani R, Begin D, Richardson L. Silica and cancer associations from a multicancer occupational exposure case-referent study. IARC Sci Publ 1990;97:29–42.
50. Parent ME, Siemiatycki J, Fritschi L. Occupational exposures and gastric cancer. Epidemiology 1998;9:48–55.
51. Finkelstein MM, Verma DK. Mortality among Ontario members of the International Union of Bricklayers and Allied Craftworkers. Am J Ind Med 2005;47:4–9.
52. Tsuda T, Mino Y, Babazono A, Shigemi J, Otsu T, Yamamoto E. A case-control study of the relationships among silica exposure, gastric cancer, and esophageal cancer. Am J Ind Med 2001;39:52–7.
53. Balarajan R, McDowall ME. Professional drivers in London: a mortality study. Br J Ind Med 1988;45:483–6.
54. Guberan E, Usel M, Raymond L, Bolay J, Fioretta G, Puissant J. Increased risk for lung cancer and for cancer of the gastrointestinal tract among Geneva professional drivers. Br J Ind Med 1992;49:337–44.
55. Kjaerheim K, Ulvestad B, Martinsen JI, Andersen A. Cancer of the gastrointestinal tract and exposure to asbestos in drinking water among lighthouse keepers (Norway). Cancer Causes Control 2005;16:593–8.
56. Kang SK, Burnett CA, Freund E, Walker J, Lalich N, Sestito J. Gastrointestinal cancer mortality of workers in occupations with high asbestos exposures. Am J Ind Med 1997;31:713–8.
57. Frumkin H, Berlin J. Asbestos exposure and gastrointestinal malignancy review and meta-analysis. Am J Ind Med 1988;14:79–95.
58. Cocco P, Palli D, Buiatti E, Cipriani F, DeCarli A, Manca P, Ward MH, Blot WJ, Fraumeni JF, Jr. Occupational exposures as risk factors for gastric cancer in Italy. Cancer Causes Control 1994;5:241–8.
59. Zandjani F, Hogsaet B, Andersen A, Langard S. Incidence of cancer among nitrate fertilizer workers. Int Arch Occup Environ Health 1994;66:189–93.
60. Krstev S, Dosemeci M, Lissowska J, Chow WH, Zatonski W, Ward MH. Occupation and risk of stomach cancer in Poland. Occup Environ Med 2005;62:318–24.
61. de Klerk NH, Armstrong BK, Musk AW, Hobbs MS. Cancer mortality in relation to measures of occupational exposure to crocidolite at Wittenoom Gorge in Western Australia. Br J Ind Med 1989;46:529–36.
62. Reid A, Ambrosini G, de Klerk N, Fritschi L, Musk B. Aerodigestive and gastrointestinal tract cancers and exposure to crocidolite (blue asbestos): incidence and mortality among former crocidolite workers. Int J Cancer 2004;111:757–61.
63. Albin M, Jakobsson K, Attewell R, Johansson L, Welinder H. Mortality and cancer morbidity in cohorts of asbestos cement workers and referents. Br J Ind Med 1990;47:602–10.
64. Knutsson A, Damber L, Jarvholm B. Cancers in concrete workers: results of a cohort study of 33,668 workers. Occup Environ Med 2000;57:264–7.
65. Ames BN, Gold LS. Too many rodent carcinogens: mitogenesis increases mutagenesis. Science 1990;249:970–1.
66. Schins RP. Mechanisms of genotoxicity of particles and fibers. Inhal Toxicol 2002;14:57–78.
67. Yoshihara M, Haruma K, Sumii K, Watanabe C, Kiyohira K, Kawaguchi H, Tanaka S, Kajiyama G. The relationship between gastric secretion and type of early gastric carcinoma. Hiroshima J Med Sci 1995;44:79–82.

EXHIBIT 9

ELSEVIER

Mutation Research 490 (2001) 179–186

Genetic Toxicology and Environmental Mutagenesis

www.elsevier.com/locate/gentox
Community address: www.elsevier.com/locate/mutres

Analysis of chromosomal aberrations in men occupationally exposed to cement dust

Shehla K. Fatima, P. Aruna Prabhavathi*, P. Padmavathi, P.P. Reddy

Institute of Genetics and Hospital for Genetic Diseases, Osmania University, Begumpet, Hyderabad (A.P.) 500016, India

Received 11 July 2000; received in revised form 21 November 2000; accepted 22 November 2000

Abstract

Cement industry is considered as a major pollution problem on account of dust and particulate matter emitted at various steps of cement manufacture. Cement dust consists of many toxic constituents. The workers who are employed in cement industries are exposed to cement dust for long periods. Therefore, it is mandatory to evaluate the mutagenic effects of occupational exposure to cement dust in such workers. In the present study, we analyzed the samples of 124 male workers including 59 smokers and 65 non-smokers who were employed in cement industry for a period of 1–17 years. For comparison, 106 controls (including 47 smokers and 59 non-smokers) of the same age group and socio-economic status were also studied. Controls had no exposure to cement dust or any known physical or chemical agent. A significant increase in the incidence of chromosomal aberrations was observed in the exposed group when compared to the control group. The results were analyzed separately for non-smokers and smokers. The chromosomal damage was more pronounced in the smokers when compared with the non-smokers both in control and exposed groups. A significant increase in the frequency of chromosomal aberrations was also observed with increase in age in both control and exposed subjects. © 2001 Published by Elsevier Science B.V.

Keywords: Cement dust; Occupational exposure; Cement industry; Chromosomal aberrations; Cytogenetic damage

1. Introduction

Rapid urbanization and industrialization in recent years has escalated the demand for cement not only in India but world wide. The accompanying growth of cement industries in India has consequently magnified the pollution problem. Cement industries are regarded to be highly-pollution prone, especially with regard to particulate emission. Therefore, it is mandatory that toxicological evaluation programs are well implemented to guard humans with exposure to cement dust against adverse health effects.

The major pollution problems in cement industry are on account of dust and particulate matter being emitted from various points like raw material grinding, coal mills, rotary kilns (dry or wet), clinker cooling, finished grinding, storage silos, and packaging. The workers in the cement industry involved in various steps of cement manufacture are worst affected and most of them get exposed to cement dust for long periods through continuous working in the cement plant. The exposure of workers to cement dust is mainly by dermal and respiratory routes and to lesser extent by ingestion.

Cement in a nutshell primarily comprises of silicates and aluminates of lime, i.e. tricalcium silicate, dicalcium silicate, tricalcium aluminate, and tetracalcium aluminoferrite. The chemical composition of cement dust reveals that it consists of toxic constituents. Therefore, it is necessary to evaluate the

* Corresponding author. Tel.: +91-81-33-13681.

1383-5718/01/$ – see front matter © 2001 Published by Elsevier Science B.V.
PII: S1383-5718(00)00165-0

occupationally-exposed population for genotoxic effects in order to assess the mutagenic potential of cement dust.

There is considerable evidence for the harmful effects of cement dust in living systems. Fleming et al. [1] reported occasional cases of emphysema and bronchitis in addition to massive collection of cement in the lung, the so-called "cementosis" among the subjects exposed to cement dust. In animal models, atrophy of elastic fibers and focal pulmonary emphysema were observed in the pulmonary tissue of rats exposed to inhalation of cement dust [2]. Kalacic [3] found the prevalence of respiratory and chronic bronchitis symptoms to be significantly higher in cement workers than in controls, both among smokers and non-smokers. Occupational bronchial asthma was also reported among cement workers [4]. A high incidence of retroflexion of the uterus, inflammation of the ovary, erosion of the vaginal part of the uterus, prolapse of the vaginal walls and incontinence was reported among women workers employed in a cement industry [5]. An increased risk of stomach cancer among cement workers was also indicated [6]. Masons handling cement were reported to have high incidence of lung cancer [7]. Laryngeal cancer also has been reported in individuals with exposure to cement dust [8,9]. In a cohort study on asbestos cement workers, high risk of colorectal tumors was observed, compared with cohorts of workers in other branches of the asbestos industry [10]. Colorectal cancers were reported to be associated with portland cement production [11]. Long-term exposure to cement dust was shown to be a risk factor for right-sided colon cancer [12].

Aluminum and silica are the prime components of cement dust. There are several reports on the adverse effects of aluminum in living systems [13,14]. Silica, an important constituent of cement dust is also reported to be toxic [15,16]. The prevalence of respiratory disease in cement industry workers in different countries varied, and some authors have attempted to correlate the noxious effects of cement dust with its free silica content [17–19].

World Health Organization (WHO) has recommended to generate data on the industrial workers to evaluate the risk to human health from exposure to chemicals or any other toxic constituents in the industries. There are several reports on the adverse effects of cement dust and its individual constituents in living systems. Cancer, besides several other respiratory disorders and skin allergies has been associated with occupational exposure to cement dust. But data on chromosomal aberration analysis on the population exposed to cement dust is rather scarce. Hence, human monitoring for genetic damage using peripheral blood lymphocytes for chromosomal abnormalities was carried out to evaluate the mutagenic potential of cement dust in the cement factory workers.

2. Materials and methods

The most extensively-employed method to assess the genetic effects of occupational exposure to mutagens has been the analysis of chromosomal alterations in stimulated peripheral blood lymphocytes in the exposed persons. Thus, cytogenetic studies were carried out in 124 males including 65 smokers and 59 non-smokers who were occupationally exposed to cement dust in the cement factory. The workers had varying duration of exposure (1–17 years) to cement dust and they were in the age group of 24–56 years. The workers did not use any protective measure while at work and were heavily powdered with cement dust by the end of their work. The 106 men including 47 smokers and 59 non-smokers who were not exposed to cement dust or any known physical or chemical agent at workplace, but belonged to the same age group and socio-economic status as that of the workers formed the control group. The subjects who smoked more than 15 cigarettes per day for at least 5 years were considered as smokers, both in exposed and control subjects.

Intravenous blood samples were collected from all the exposed and control subjects, and whole blood 72 h cultures were initiated in RPMI 1640 medium supplemented with 25% AB serum, 0.5% phytohaemagglutinin-P, and 0.25% antibiotic. Colchicine (0.1 ug/ml) was added 2 h before harvesting the cultures to arrest the cell cycle at metaphase stage. Cultures were harvested, slides were prepared according to the standard method of Moorhead et al. [20] with slight modifications suitable to the laboratory conditions. All the slides were stained with giemsa and were coded. The 150 well-spread metaphases were screened for each sample for various structural and numerical types of aberrations by two researchers independently.

The results were analyzed separately for the non-smokers and smokers. The statistical analysis of the data was done using χ^2 test and two-way ANOVA with post-hoc test to assess the effects of cement dust, smoking habits, and age of the individuals on chromosomal damage.

3. Results

The 124 male workers (65 smokers and 59 non-smokers) who were occupationally exposed to cement dust in the cement factory for varying durations of time were studied for the analysis of chromosomal aberrations. The results (for both non-smokers and smokers) are presented in Tables 1 and 2.

- Non-smokers: cytogenetic studies were carried out in 59 male workers who were non-smokers and occupationally exposed to cement dust in the cement factory. For comparison, 59 males who were non-smokers and not exposed to cement dust or any other physical or chemical agent and belonging to the same socio-economic status were selected for study as control group (C-I). The results of this study are presented in Table 1.

  Table 1 represents the data on chromosomal aberrations. There was an increase in the frequency of chromatid aberrations and chromosomal aberrations in non-smokers exposed to cement dust when compared to the control group (C-I). The chromatid gaps, breaks, acentric fragments and exchanges were 2.37, 1.42, 0.87, and 0.01% in the exposed group as against 0.85, 0.41, 0.15, and 0.0% in the control group (C-I), respectively. The frequency of isochromatid gaps, breaks, acentric fragments were 0.44, 0.34, and 0.52% in the exposed group when compared to 0.0, 0.01, and 0.03% in the control group (C-I), respectively. The frequency of polyploids and dicentrics were 0.89 and 0.66% in the exposed group, respectively, while no polyploids or dicentrics were recorded in the control group (C-I). The total chromosomal aberrations excluding gaps and polyploids were 3.82% in the exposed group as against 0.60% in control group (C-I). With increase in duration of exposure to cement dust, a relative increase in the frequency of chromosomal aberrations was observed. The total aberrations were 3.13, 4.04, and 4.89% in non-smokers exposed to cement dust for 1–5, 6–11, and 12–17 years, respectively, when compared to the percentage frequency of 0.60 in the control group (C-I).
- Smokers: 65 male smokers exposed to cement dust were analyzed for chromosomal aberrations. Besides exposed individuals, 59 non-smokers (C-I) and 47 smokers (C-II) who were not exposed to cement dust or any other physical or chemical agent at workplace were also studied. The data of the smoker exposed group were compared with that of the smoker control group (C-II). The results of the above study are given in Table 2.

  The results show an increase in the incidence of chromosomal aberrations in the smoker control group (3.62%) when compared to the non-smokers of the control group (0.60%). The exposed group showed an approximate two-fold increase (7.08%) in the total number of aberrations when compared to the control group (3.62%, C-II). The chromatid gaps, breaks, acentric fragments and exchanges were 2.62, 1.56, 1.80, and 0.03% in the exposed group as against 1.90, 1.26, 1.50, and 0.0% in the control group (C-II), respectively. The frequencies of isochromatid gaps, breaks, acentric fragments were 0.87, 0.66, and 1.66% in the exposed group when compared to 0.06, 0.04, and 0.21% in the control group (C-II), respectively. In the exposed group, the frequency of polyploids was 1.53% as against 0.31% in the control group (C-II), while the frequency of dicentrics was 1.37% as against 0.60% in the control group (C-II).

  The data were further analyzed based on the duration of exposure to cement dust in the workers. As the duration of exposure to cement dust increased, there was a corresponding increase in the frequency of chromosomal aberrations. The total chromosomal aberrations were 5.94, 7.39, and 8.52% in the groups exposed to cement dust for 1–5, 6–11, and 12–17 years, respectively, as against 3.62% in the control group (C-II).

3.1. Statistical significance

The increase in the frequencies of aberrations in both non-smokers and smokers of the exposed group was statistically significant when compared with

Table 1
Frequency of chromosomal aberrations in non-smokers exposed to cement dust in cement factory[a]

Group	Number of samples	Number of metaphases screened	Chromatid aberrations				Isochromatid aberrations				Total number of aberrations[b] ±S.E.	Number of polyploid cells
			Gaps	Breaks	Acentric fragments	Exchanges	Gaps	Breaks	Acentric fragments	Dicentrics		
Control group-I	59	8850	75 (0.85)	36 (0.41)	13 (0.15)	0.0	0.0	1 (0.01)	3 (0.03)	0.0	53 (0.60) ± 0.08	0.0
Exposed group duration of exposure (years)												
1–5	20	3000	60 (2.0)	36 (1.20)	23 (0.77)	0.0	12 (0.40)	9 (0.30)	11 (0.37)	15 (0.50)	94* (3.13) ± (0.32)	16 (0.53)
6–11	33	4950	123 (2.48)	74 (1.49)	45 (0.91)	0.0	22 (0.44)	17 (0.34)	29 (0.59)	35 (0.71)	200* (4.04) ± 0.28	49 (0.99)
12–17	6	900	27 (3.0)	16 (1.78)	9 (1.0)	1.0 (0.11)	5 (0.56)	4 (0.44)	6 (0.67)	8 (0.89)	44* (4.89) ± 0.72)	14 (1.56)
Total 1–17	59	8850	210 (2.37)	126 (1.42)	77 (0.87)	1 (0.01)	39 (0.44)	30 (0.34)	46 (0.52)	58 (0.66)	338* (3.82) ± 0.20	79 (0.89)

[a] 150 Metaphases were analyzed for each sample. Values given in parentheses are percentages.
[b] Gaps and polyploids are not included in total number of aberrations.
* $P < 0.05$.

Table 2
Frequency of chromosomal aberrations in smokers exposed to cement dust in cement factory[a]

Group	Number of samples	Number of metaphases screened	Chromatid aberrations				Isochromatid aberrations				Total number of aberrations[b] ±S.E.	Number of polyploid cells
			Gaps	Breaks	Acentric fragments	Exchanges	Gaps	Breaks	Acentric fragments	Dicentrics		
Control group-I	59	8850	75 (0.85)	36 (0.41)	13 (0.15)	0.0	0.0	1 (0.01)	3 (0.03)	0.0	53 (0.60) ± 0.08	0.0
Control group-II	47	7050	134 (1.90)	89 (1.26)	106 (1.50)	0.0	4 (0.06)	3 (0.04)	15 (0.21)	42 (0.60)	255* (3.62) ± 0.22	22 (0.31)
Exposed group duration of exposure (years)												
1–5	21	3150	69 (2.19)	41 (1.30)	50 (1.59)	0.0	22 (0.70)	16 (0.51)	47 (1.49)	33 (1.05)	187* (5.94) ± (0.42)	39 (1.24)
6–11	35	5250	141 (2.69)	84 (1.60)	99 (1.89)	1.0 (0.02)	48 (0.91)	36 (0.69)	89 (1.70)	79 (1.50)	388* (7.39) ± 0.36	84 (1.60)
12–17	9	1350	45 (3.33)	27 (2.0)	26 (1.93)	2.0 (0.15)	15 (1.11)	12 (0.89)	26 (1.93)	22 (1.63)	115* (8.52) ± 0.76)	26 (1.93)
Total 1–17	65	9750	255 (2.62)	152 (1.56)	175 (1.80)	3.0 (0.03)	85 (0.87)	64 (0.66)	162 (1.66)	134 (1.37)	690* (7.08) ± 0.26	149 (1.53)

[a] 150 Metaphases were analyzed for each sample. Values given in parentheses are percentages.
[b] Gaps and polyploids are not included in total number of aberrations.
* $P < 0.05$.

Table 3
Chromosomal aberrations in different age groups for the given smoking habits[a]

Group	Age	Mean number of aberrations per sample	S.D.	Sample size
Non-smoker				
Control group (C-I)	≤30	0.677	0.638	34
	31–40	1.167	0.5774	12
	≥41	1.231	0.4385	13
	Total	0.898	0.6350	59
Exposed group	≤30	4.524	1.940	21
	31–40	6.129	2.473	31
	≥41	7.571	1.512	7
	Total	5.729	2.391	59
Smoker				
Control group (C-II)	≤30	4.524	2.839	21
	31–40	5.313	2.330	16
	≥41	7.500	1.509	10
	Total	5.426	2.652	47
Exposed group	≤30	8.348	2.014	23
	31–40	11.600	1.370	33
	≥41	12.778	2.539	9
	Total	10.402	2.321	65

[a] Between the groups for the given smoking habits: F-ratio 182.9, $P < 0.001$; between the age groups: F-ratio 29.2, $P < 0.001$; between the groups for the given smoking habits and age: F-ratio 4.3, $P < 0.001$.

the values observed in the respective control groups ($P < 0.05$). The frequency of aberrations in the non-smoker and smoker exposed groups at all the time intervals was statistically significant when compared with the respective control values ($P < 0.05$). The differences in the frequencies of chromosomal aberrations in between all the time intervals were significant except between 6–11 and 12–17 years groups.

Data were also analyzed according to the age and smoking habits of the exposed and control subjects to evaluate the effect of age and smoking on the incidence of chromosomal aberrations (Table 3). Statistical analysis by two-way ANOVA with post-hoc test revealed significant increase in age both in control and exposed subjects. The differences in the mean number of aberrations in between all the age groups (≤30 versus 31–40, ≤30 versus ≥41, 31–40 versus ≥41 years), and between smokers and non-smokers in control and exposed groups were also statistically significant ($P < 0.001$).

4. Discussion

In recent years, there has been a phenomenal increase in the quantity of cement being produced in India. While the growth of the cement industry is proving a matter of great benefit for the average man, this growth has also considerably increased the health hazard in the form of environmental pollution. Cement industry is perhaps the biggest single industry creating the maximum amount of pollution of the atmospheric air. The dust generated in various processes of cement manufacture right from processing of the raw materials up to bagging causes adverse effects on the health of cement plant workers. There are several reports on the adverse effects of cement dust in animals [21,22]. Pulmonary disorders [23,24], carcinogenesis [7–9,11,12], and liver abnormalities [25] have been reported among cement factory workers.

In the present study, the type of aberrations observed in exposed and control populations were gaps, breaks, fragments of chromatid and chromosome types. Exchanges, dicentrics, and polyploids were recorded only in the exposed group. However, gaps were not included in total number of aberrations, since gaps are termed as achromatic lesions and remain unstained by the Feulgen techniques [26,27]. According to Brogger [28], the gaps observed in metaphase chromosomes are the result of insufficient folding of chromosome fibers. The genetic importance of gaps is neither well defined nor understood [29], yet they are considered as important in the present analysis, since they affect the basic chromosome structure.

Aluminum is one of the prime components of cement dust. Earlier reports have established the cytogenetic effects of aluminum compounds in living systems. Chromosome aberrations (gaps, breaks, failure of pairing) were produced in spermatocytes of grasshoppers (*Phloeoba antnnata*) fed on standard Drosophila food mixed with 10 mg of aluminum chloride per 0.21 g body weight and examined 48 or 60 h later [30]. Manna and Das [31] reported increased structural chromosome aberrations in the bone marrow of mice injected with 1 ml (per 30 g of body weight) of 0.01–0.1 M solutions of aluminum chloride. Aluminum is known to have high affinity for DNA and RNA [32], and its interaction with microtubule aggregation in vitro [33] may result in clastogenic effects and increased SCEs. Ajoy et al.

[14] and others have reported an increase in the frequency of chromosomal aberrations and SCEs in the peripheral blood lymphocytes treated with aluminum sulphate (in vitro).

Chromium is present in the finished cement, although the raw materials used for the manufacture of cement do not usually contain chromium. The possible source of chromium in finished cement could be the abrasions of refractory lining of the kiln and steel balls used in mills [35]. Bigaliev et al. [34] confirming the previous observations in animals reported an increase in the incidence of chromosomal aberrations in persons engaged in chromium production [36]. Positive results and dose-related increase in chromosomal aberrations and sister-chromatid exchanges have been reported with the following hexavalent chromium compounds: CrO_3 [37], $K_2Cr_2O_7$ [38], K_2CrO_4 [38]. Thus, in portland cement, hexavalent chromium which is an established carcinogen further corroborates the genetic damage caused by cement dust.

The frequency of total chromosomal aberrations was significantly higher in smoker control group when compared to the non-smoker control group, suggesting that smoking causes chromosomal damage. There are several reports on chromosomal damage among smokers. Our results are in accordance with other reports [39–42] which presented evidence for an increased frequency of chromosomal aberrations in lymphocytes of smokers and alcoholics. Littlefield and Joiner [43] studied chromosomal aberrations in lymphocytes of long-term heavy smokers, and reported high frequencies of dicentrics, translocations, and chromatid exchanges in smokers when compared to non-smokers.

The overall observations of the study clearly showed chromosomal damage in the somatic cells of workers (both smokers and non-smokers) occupationally exposed to cement dust for several years. Similar effects were also reported among workers who are occupationally exposed to other chemicals in factories [44], hospitals [45], agricultural fields [46], etc. The workers are exposed to various oxide components of cement such as calcium, aluminum, silica, iron, titanium, chromium, etc. and hence it is difficult to pin-point a particular element responsible for chromosomal damage. The clastogenic effects in the workers might be attributed to the cumulative effect of these components. The effects are more pronounced in smokers and in older age groups indicating that these groups run a higher risk for genetic damage.

Acknowledgements

P. Padmavathi and P.A. Prabhavathi acknowledge the financial assistance from CSIR, New Delhi.

References

[1] A.J. Fleming, A. D'Alonzo, J.A. Zapp, Modern. Occup. Med., 2nd Edition, Lea and Febiger, 1960.
[2] W. Niepolomski, M. Sosnierz, M. Wieozorek, Obraz patomorfologiezny narzadu odd echowego W doswiad-ozalnej pylicy cementowej U szezurow, Medycynapracy 18 (1967) 369.
[3] I. Kalacic, Chronic nonspecific lung disease in cement workers, Arch. Environ. Health 26 (1973) 78–83.
[4] L.M. Malceva, L.A. Tatanov, Professional 'nye zabolevanija organov dyhanija V uslovijah sovremennogo cementogo proizvodstva, Gigiena Truda i professional 'nye zabolevanija 3 (1974) 14.
[5] J. Dudkiewicz, K. Kaminiski, A. Rybozynska, Preventive gynaecological examination of women employed in cement industry, Med. Pr. 34 (1) (1983) 89–94.
[6] M.E. Mc Dowall, A mortality study on cement workers, Br. J. Ind. Med. 41 (1984) 179–182.
[7] V. Rafnsson, S.G. Johannesdottir, Mortality among masons in Iceland, Br. J. Ind. Med. 43 (1986) 522–525.
[8] J. Olsen, S. Sabroe, Occupational causes of laryngeal cancer, J. Epidemiol. Community Health 38 (1984) 117–121.
[9] H. Maier, A. Dietz, D. Zielinski, K.H. Junemann, W.D. Heller, Riskofactoren bei Plattenepithelkaizinomess der Mundhohle, des oropharynx, des Hypopharynx und des Larynx, Dtsch. Med. Wochenschr 115 (1990) 843–850.
[10] M. Albin, K. Jakobsson, R. Attewell, L. Johansson, H. Wellinder, Mortality and cancer morbidity in cohorts of asbestos cement workers and referents, Br. J. Ind. Med. 47 (1990) 602–610.
[11] K. Jakobsson, R. Attewell, B. Hultgren, K. Sjoland, Gastrointestinal cancer among cement workers — a case referent study, Int. Arch. Occup. Environ. Health 62 (1990) 337–340.
[12] K. Jakobsson, V. Horstmann, H. Welinder, Mortality and cancer morbidity among cement workers, Br. J. Ind. Med. 50 (1993) 264–272.
[13] R.M. Garruto, R. Fukatsu, R. Yanagihara, D.C. Gajdusek, G. Hook, C.E. Flori, Imaging of calcium and aluminium in neurufibrillary tangle-bearing neurons in parkinsonism-dementia of Guams, Proc. Natl. Acad. Sci. U.S.A. 81 (1984) 1875–1879.
[14] K.R. Ajoy, T. Geeta, S. Archana, Effects of aluminium sulphate on human leukocyte chromosomes in vitro, Mutat. Res. 244 (1990) 179–183.

[15] Y. Oghiso, Y. Yamada, Y. Shibata, Effects of instilled fibrogenic particles on the clonal growth of murine pulmonary alveolar macrophages, Environ. Health Perspect. 97 (1992) 159–161.
[16] H.S. Koren, M. Joyce, R.B. Devlin, S. Becker, K. Driscoll, M.C. Madden, Modulation of eicosanoid production by human alveolar macrophages exposed to silica in vitro, Environ. Health Perspect. 97 (1992) 77–83.
[17] H.J. Einbrodt, D. Hentschel, Tierexperimentelle Untersuchungen mit Arbeitsplatzstauben aus cinem Huttenzementwerk, Int. Archiv Fur Gewerbepathologic Gewerbehygiene 22 (1966) 354–366.
[18] P. Hublet, Enquete relative a resque de pneumoconiose dans la fabrication des liments de construction, Archieves Belges de Medecine sociale, Hygiene, Medecine du Travail et Medecine Legale 26 (1968) 417–430.
[19] W.R. Parkes, Occupational Lung Disorders, Butterworths, London, 1974, pp. 157–159, 346–347.
[20] P.S. Moorhead, P.C. Nowell, W.J. Mellman, D.M. Battips, D.A. Hungerford, Chromosome preparations of leucocytes cultured from human peripheral blood, Exp. Cell. Res. 20 (1960) 613–616.
[21] K. Kolev, G. Sumkov, Varbu biologicnoto Vazdejstvie na cimentovija prah pri intraperi tonealnija I intra haalnija test, Problemi na Higienata 1 (1975) 111.
[22] H. Wozniak, E. Wiecek, The effect of asbestos cement, cement and asbestos dusts on the lungs of rats, Med. Pr. 35 (1984) 269–272.
[23] J. Vyskocil, Dloubodobe sledovani Vyvoje Vlekle brcnchidity u cement arenskych delniku, Vnitrni Lekarstvi 14 (1968) 341.
[24] A. Maciejewska, G. Bielichowska-cybula, Biological effect of cement dust, Med. Pr. 42 (1991) 281–289.
[25] J. Cortez Pimental, A. Peixoto Menezes, Pulmonary and hepatic granulomatous disorders due to the inhalation of cement and micadust, Thorax 33 (1978) 219–227.
[26] G. Obe, Die wirkung von streptomycin und dihydrostreptomycin auf menschiliche chromosome in vitro, Mol. Gen. Genet. 107 (1970) 361–365.
[27] R. Rieger, A. Michaelis, M.M. Green, Glossary of Genetics and Cytogentics, Springer, Berlin, 1976.
[28] A. Brogger, Apparently spontaneous chromosome damage in human leucocytes and the nature of chromatid gaps, Humangentik 13 (1971) 1–4.
[29] L. Schoeller, U. Wolf, Possibilities and limitations of chromosomes treated in vitro for the problem of chemical mutagenesism, in: F. Vogal, G. Rohrborn (Eds.), Chemical Mutagenesis in Mammals and Man, Springer, Berlin, 1970, pp. 232–250.
[30] G. Manna, B.B. Parida, Aluminium chloride induced meiotic chromosome aberrations in the grasshopper *Phloeoba antnnata*, Naturwissenchaften 52 (1965) 647–648.
[31] G. Manna, R.K. Das, Chromosome aberrations in mice induced by aluminium chloride, Nucleus 15 (1972) 180–186.
[32] D. Dyrssen, C. Haraldsson, E. Nyberg, M. Wedberg, Complexation of aluminium with DNA, J. Inorg. Biochem. 29 (1987) 67–75.
[33] T.L. Mac Donald, W.G. Humphreys, R.B. Martin, Promotion of tubulin assembly by aluminium ion in vitro, Science 236 (1987) 183–186.
[34] L. Prodan, Cement, Occupational Health and Safety, Vol. 1, Geneva, International Labour Office.
[35] A.B. Bigaliev, M.N. Turebaev, R.K. Bigalieva, M.Sh. Elemesova, Cytogenetic examination of workers engaged in chrome production, Genetika 13 (1977) 545.
[36] M. Umeda, M. Nishimura, Inducibility of chromosomal aberrations by metal compounds in cultured mammalian cells, Mutat. Res. 67 (1979) 221–229.
[37] W.D. Mac Rae, R.F. Whiting, H.F. Stich, Sister chromatid exchanges induced in cultured mammalian cells by chromate, Chem. Bio. Interact. 26 (1979) 281–286.
[38] IARC, Some metals and metallic compounds, IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, International Agency for Research on Cancer, Lyon, Vol. 23, 1980, pp. 205–323.
[39] G. Obe, J. Herha, Chromosomal aberrations in heavy smokers, Hum. Genet. 41 (1978) 259–263.
[40] H.J. Evans, Induction of aberrations in human chromosomes following exposure to mutagens/carcinogens, in: P. Emm, E. Krick (Eds.), Environmental Carcinogenesis, Elsevier, Amsterdam, 1979, pp. 329–344.
[41] G. Obe, Ristow, Mutagenic, carcinogenic and teratogenic effects of alcohol, Mutat. Res. 65 (1979) 229–259.
[42] G. Obe, D. Gobal, H. Engeln, J. Herha, A.T. Natarajan, Chromosomal aberrations in peripheral lymphocytes of alcoholics, Mutat. Res. 73 (1980) 377–386.
[43] L.G. Littlefield, E.E. Joiner, Analysis of chromosome aberrations in lymphocytes of longterm heavy smokers, Mutat. Res. 170 (1986) 145–150.
[44] M. Hemaprasad, K. Pushpavathi, P.P. Reddy, Cytogenetic damage in lymphocytes of rubber industry workers, Environ. Res. 40 (1986) 199–201.
[45] P. Padmavathi, P.A. Prabhavathi, M. Hemaprasad, S.K. Fatima, P.P. Reddy, Chromosomal aberrations in operating theatre staff, Med. Sci. Res. 23 (1995) 279–280.
[46] D.S. Rupa, P. Rita, P.P. Reddy, O.S. Reddi, Screening of chromosomal aberrations and sister chromatid exchanges in peripheral blood lymphocytes of vegetable garden workers, Hum. Toxicol. 7 (1988) 333–336.

EXHIBIT 10

UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY
REGION IX

In the Matter of:	)	
	)	
LEHIGH SOUTHWEST CEMENT COMPANY	)	Docket No. R9-10-02
	)	NOTICE OF VIOLATION
Proceeding under Section 113(a)	)	AND FINDING OF
of the Clean Air Act,	)	VIOLATION
42 U.S.C. § 9613(a)	)	
	)	

NOTICE OF VIOLATION/FINDING OF VIOLATION

This Notice of Violation and Finding of Violation ("NOV/FOV") is issued to the Lehigh Southwest Cement Company ("Lehigh") for violations of the Clean Air Act ("CAA" or the "Act"), as amended, 42 U.S.C. §§ 7401-7671q, at its Portland cement manufacturing facility located in Cupertino, California (the "Facility"). Lehigh violated the Prevention of Significant Deterioration ("PSD") and Title Operating Permit Program requirements of the Act at the Facility. This NOV/FOV is issued pursuant to Sections 113(a)(1), 113(a)(3) and 167 of the Act. Section 113(a)(1) requires the Administrator of the United States Environment Protection Agency ("EPA") to notify any person she finds in violation of an applicable implementation plan or a permit. The federal PSD regulations also clarify that failure to comply with the PSD provisions renders a source subject to enforcement under Section 113 of the Act. *See* 40 C.F.R. § 52.23. The authority to issue this NOV has been delegated to the Regional Administrator of EPA Region 9 and further re-delegated to the Director of the Air Division in EPA Region 9.

SUMMARY OF VIOLATIONS

The Facility is a Portland cement manufacturing plant comprised of one kiln, and associated equipment used to produce clinker, including a preheater tower, precalciner, clinker cooler, induced draft ("ID") and other fans, cement finish mills, and extensive sections of ductwork.

This NOV/FOV concerns a series of physical modifications made to the Facility from 1996 through 1999. Lehigh subsequently operated the Facility with the modified equipment which resulted in significant net emission increases. As a result, the projects, either individually or in the aggregate, caused an increase in production of cement and an increase in emissions of air pollutants to the atmosphere from the Facility.

The Facility is located in an area that has at all relevant times been classified as attainment for nitrogen dioxide ("NO_2") and sulfur dioxide ("SO_2"). Accordingly, the PSD provisions of Part C, Title I of the Act apply to operations at the Facility for oxides of nitrogen ("NO_x")[1] and SO_2 emissions. EPA has determined that the physical or operational changes identified in this NOV/FOV, either individually or in the aggregate, were major modifications for PSD purposes since the Facility significantly increased both actual and potential emissions of NO_x and SO_2 as a result of the changes. Moreover, Lehigh failed to apply for one or more PSD permits for the modifications covering NO_x and SO_2

[1] NO_2 serves as the regulated pollutant for the NO_2 standard.

emissions. Lehigh's failure to apply for a PSD permit or install and operate additional emissions controls meeting best available control technology ("BACT") covering these pollutants when it constructed and began operating the physical or operational changes was a violation of the PSD requirements of the Act.

Lehigh has also violated the Title V Operating Permit Program requirements of the Act set forth at 42 U.S.C. §§ 7461-7661f, the federal Title V regulations set forth at 40 C.F.R. Part 70, and the approved Bay Area Air Quality Management District ("BAAQMD") Title V program set forth at Regulation 2 Rule 6. BAAQMD has administered an approved Title V Operating Permit Program since November 29, 1994. Lehigh's failure to identify PSD requirements in its application submitted to BAAQMD for a Title V permit, supplement or correct that application to include PSD requirements, or obtain a Title V permit that contains the PSD requirements after the construction and operation of the physical or operational changes are violations of Title V requirements. *See* 42 U.S.C. §§ 7661b(a)-(b) and 7661c(a); 40 C.F.R. §§ 70.5(a)(c); BAAQMD Regulation 2 Rule 6. As a result, Lehigh obtained a deficient Title V permit, i.e., one that did not include all applicable requirements, and therefore is operating the Facility without a valid Title V permit in violation of 42 U.S.C. §§ 7661a, 7661b, and 7661c; 40 C.F.R. §§ 70.1, 70.5 and 70.6; and BAAQMD Regulation 2 Rule 6.

STATUTORY & REGULATORY BACKGROUND

National Ambient Air Quality Standards

1. The Administrator of EPA, pursuant to authority under Section 109 of the Act, 42 U.S.C. § 7409, has promulgated National Ambient Air Quality Standards ("NAAQS") for certain criteria pollutants relevant to this NOV/FOV, including NO_2 and SO_2. *See* 40 C.F.R. §§ 50.4, 50.5, 50.7, 50.8, 50.9, and 50.10.

2. Pursuant to Section 107(d) of the Act, 42 U.S.C. § 7407(d), the Administrator promulgated lists of attainment status designations for each air quality control region ("AQCR") in every state. These lists identify the attainment status of each AQCR for each of the criteria pollutants. The attainment status designations for the California AQCRs are listed at 40 C.F.R. §§ 81.305.

Prevention of Significant Deterioration

3. Section 110 of the Act, 42 U.S.C. § 7410, requires each state to adopt and submit to EPA a plan that provides for the implementation, maintenance and enforcement of primary and secondary NAAQS in the state. Upon approval by EPA, the plan becomes part of the applicable state implementation plan ("SIP") for that state.

4. Section 110(a)(2)(C) of the Act, 42 U.S.C. § 7410(a)(2)(C), requires that each SIP include a PSD permit program as provided in Part C of Title I of the Act, 42 U.S.C. §§ 7470-7491. Part C sets forth requirements for SIPs for attainment areas to ensure maintenance of the NAAQS.

5. On June 19, 1978, pursuant to Sections 160 through 169 of the Act, 42 U.S.C. §§ 7470-7479, EPA promulgated federal PSD regulations at 40 C.F.R. § 52.21. 43 Fed. Reg. 26,402.

6. The federal PSD program was incorporated into all applicable implementation plans nation-wide and contains the applicable PSD program requirements for each plan until EPA approves into an individual SIP a replacement program. See 40 C.F.R. § 52.21(a); 42 U.S.C. § 7410(a)(2)(C).

7. Pursuant to Section 107(d) of the Act, 42 U.S.C. § 7407(d), the Administrator promulgated lists of attainment status designations for each AQCR in every state. These lists identify the attainment status of each AQCR for each of the criteria pollutants. The NO_2 and SO_2 attainment status designations for the California AQCRs are listed at 40 C.F.R. § 81.305.

8. The BAAQMD has primary jurisdiction over major stationary sources of air pollution sources in the San Francisco Bay Area Intrastate AQCR. 40 C.F.R. § 81.21. This jurisdiction includes the Facility.

9. Section 161 of the Act, 42 U.S.C. § 7471, requires that each SIP contains provisions to implement the Act's PSD program for areas of that state which are designated as being in attainment with any NAAQS for a criteria pollutant. The PSD program applies to major new sources of air pollution.

10. The PSD permitting program for the San Francisco Bay Area Intrastate AQCR is the federal PSD program, which is set forth at 40 C.F.R. § 52.21.

11. Subsequent to 1978, the PSD regulations have been periodically revised. As the PSD violations identified in this NOV/FOV first commenced from 1991 through 2003, the 1992 amendments to the PSD regulations contain the applicable provisions pertaining to the alleged violations identified in this NOV/FOV. *See* 57 Fed. Reg. 32314 (July 21, 1992).

12. 40 C.F.R. § 52.21 (b)(1)(i)(a) (1992) defined a "major stationary source" as any stationary source within one of 28 source categories which emits, or has the potential to emit, 100 tons per year ("tpy") or more of any air pollutant subject to regulation under the Act. Portland cement plants are included among the 28 source categories.

13. The PSD Regulations defined a "major modification" as "any physical change in or change in the method of operation of a major stationary source that would result in a significant net emissions increase of any pollutant subject to regulation under the Act." 40 C.F.R. § 52.21(b)(2)(i) (1992).

14. 40 C.F.R. § 52.21(b)(3)(i) (1992) defined "net emissions increase" as the "amount by which the sum of the following exceeds zero:

a. Any increase in actual emissions from a particular physical change or change in the method of operation at a stationary source; and

b. Any other increases and decreases in actual emissions at the source that are contemporaneous with the particular change and otherwise creditable."

15. 40 C.F.R. § 52.21(b)(21) (1992) defined "actual

emissions" as follows: "In general, actual emissions as of a particular date shall equal the average rate, in tons per year, at which the unit actually emitted the pollutant during a two-year period which precedes the particular date and which is representative of normal source operation." The PSD regulations also provide that "[f]or any emissions unit ... which has not begun normal operations on the particular date, actual emissions shall equal the potential to emit on that date." 40 C.F.R. § 52.21(b)(21)(IV) (1992).

16. 40 C.F.R. § 52.21(b)(4) (1992) defined "potential to emit" as the "maximum capacity of a stationary source to emit a pollutant under its physical or operational design. Any physical or operational limitation on the capacity of the source to emit a pollutant, including the air pollution control equipment and restrictions on hours of operation or on the type or amount of material combusted, stored, or processed, shall be treated as part of its design if the limitation or the effect it would have on emissions is federally enforceable."

17. As such, the PSD regulations utilize an actual-to-potential test to determine whether an emissions increase occurred. Moreover, 40 C.F.R. § 52.21(b)(23)(i) (1992) defined "significant" and states that, in reference to NO_x and SO_2, significant net emissions increase means an increase that would equal or exceed 40 tons or more per year.

18. An applicant for a PSD permit to modify a stationary source is required to submit all information necessary to allow the permitting authority to perform any analysis or make any

determination required in order to issue the appropriate permit. 40 C.F.R. § 52.21(n) (1992).

19. 40 C.F.R. § 52.21(i) (1992) prohibited commencement of actual construction of a major modification to which the PSD requirements apply unless the source had a permit stating that the requirements of 40 C.F.R. §§ 52.21(j)-(r) had been met.

20. The PSD permitting process required, among other things, that for pollutants emitted in significant amounts, the owner or operation of a major source apply BACT to control emissions, 40 C.F.R. § 52.21(j) (1992); model air quality, 40 C.F.R. § 52.21(l) (1992); and perform a detailed impact analysis regarding both the NAAQS and allowable increments, 40 C.F.R. § 52.21(k) (1992).

21. Any owner or operator of a source or modification subject to 40 C.F.R. § 52.21 who commenced construction after the effective date of the PSD regulations without applying for and receiving a PSD permit is subject to appropriate enforcement action by EPA. 40 C.F.R. § 52.21(r)(1) (1992); Sections 113 and 167 of the Act, 42 U.S.C. §§ 7413 and 7477.

Title V Operating Permit Program

22. Title V of the Act, 42 U.S.C. §§ 7661-7661f, establishes an operating permit program for "major sources," including any source required to have a PSD permit. *See* Section 502(a) of the Act, 42 U.S.C. § 7661a(a). Regulations implementing the Title V permit program are set forth in 40

C.F.R. Part 70.

23. Pursuant to Title V, it is unlawful for any person to violate any requirement of a permit issued under Title V or to operate a major source except in compliance with a permit issued by a permitting authority under Title V. Section 502(a) of the Act, 42 U.S.C. § 7661a(a).

24. Under Section 502(d)(1) of the Act, states were required to develop and obtain approval to administer Title V programs. 42 U.S.C. § 7661a(d)(1). EPA granted interim approval of BAAQMD's Title V Operating Permit Program effective July 24, 1995, and final full approval was effective November 30, 2001. See 40 C.F.R. Part 70 Appendix A.

25. Sources subject to Title V and falling under BAAQMD's jurisdiction are required to submit to BAAQMD timely and complete Title V applications that identify, among other things, all "applicable requirements," including PSD requirements. *See* 40 C.F.R. § 70.5(a); BAAQMD Rule 2-6-404 and 2-6-405.

26. Sources subject to Title V and falling under BAAQMD's jurisdiction who have submitted an application are required to supplement or correct the application to include applicable requirements that were not included in the original application. 40 C.F.R. § 70.5(b); BAAQMD Rule 2-6-405.10.

27. Sources subject to Title V and falling under BAAQMD jurisdiction must obtain a Title V permit that: 1) contains such conditions necessary to assure compliance with the applicable

requirements; 2) identifies all applicable requirements the source is subject to; and 3) certifies compliance with all applicable requirements, and 4) where a source is not meeting requirements, contains a plan for coming into compliance. Sections 503 and 504 of the Act, 42 U.S.C. §§ 7661b and 7661c(a); 40 C.F.R. §§ 70.1, 70.5 and 70.6; BAAQMD Rule 2-6-409.

28. Failure of a source subject to Title V to submit a complete application; supplement that application when new requirements become applicable, or to obtain a Title V permit that contains all applicable requirements, such as PSD requirements, are violations of the Act.

FINDINGS OF FACT

29. The Facility is a Portland cement manufacturing facility, which is located at 24001 Stevens Creek Boulevard, Cupertino, Santa Clara County, California.

30. The San Francisco Bay Area Air Basin, which includes Santa Clara County where the Facility is located, was designated as attainment/unclassifiable at all times for NO_2 and SO_2 by operation of law under Sections 107(d)(1)(C) and 186(a) of the Act, 42 U.S.C. §§ 7407(d)(1)(C) and 7486(a). *See* 56 Fed. Reg. 56694 (Nov. 6, 1991); 40 C.F.R. § 81.305.

31. Lehigh is the current owner and operator of the Facility. The Facility was formerly owned by Hanson Permanente Cement and Kaiser Cement Corporation.

32. The Facility includes one kiln, and associated

equipment used to produce clinker, including a preheater tower, precalciner, clinker cooler, induced draft ("ID") and other fans, cement finish mills, and extensive sections of ductwork.

33. The combustion of coal, petroleum coke, and natural gas at the kiln at the Facility produces emissions of NO_x and SO_2, which are released to the atmosphere through a collection of 32 individual mini-stacks exiting from the baghouse.

34. Between 1996 and 1999, Lehigh commenced construction of various physical and/or operational changes at the Facility, and has continued to operate the Facility with these modifications, including, but not limited to, the following:

a. Upgrades to the finish mill; and

b. Various other modifications, upgrades, and operational changes *[Note: The underlying documents identifying these other projects have been claimed by Lehigh as confidential business information, and therefore are not being specifically identified in this NOV/FOV. Regardless, as the NOV/FOV raises allegations relating to all physical or operational changes commencing from 1996 through 1999, these other projects are covered within the scope of the NOV/FOV.]*.

35. Lehigh intended that these physical or operational changes, either individually or in the aggregate, would increase the production capacity of the Facility.

36. These physical or operational changes, either

individually or in the aggregate, resulted in an increase in annual clinker production at the Facility.

Prevention of Significant Deterioration

37. The Title V Permit issued by BAAQMD included, among other conditions, the following annual emissions limits for NO_x and SO_2 emissions from the Kiln at the Facility:

	NO_x	SO_2
Emissions limit (tpy)	5,072	2,106.8

38. As the limits in the Title V Permit for the Facility are federally enforceable, they constitute the Facility's Potential to Emit ("PTE").

39. Based upon a comparison of pre-construction actual emissions to post-construction PTE, the physical or operational changes identified in Paragraph 34, either individually or in the aggregate, resulted in net emissions increases from the Facility of NO_x and SO_2.

40. The net emissions increases of NO_x and SO_2 as a result of the physical or operational changes identified in Paragraph 34, either individually or in the aggregate, constitute a PSD significant net emissions increase since the increases were above 40 tpy for NO_x and SO_2.

41. Each of the physical or operational changes identified in Paragraph 34 constituted, either individually or in the aggregate, a "major modification" to the Facility for PSD purposes, as defined by 40 C.F.R. § 52.21 (b)(2)(i).

42. Lehigh did not apply for a PSD Permit covering NO_x and

SO_2 emissions for any of the physical or operational changes identified in Paragraph 34.

43. Lehigh failed to install and operate BACT-level emission controls for NO_x and SO_2 emissions from the Facility either at the time each of the physical or operational changes identified in Paragraph 34 were commenced or any time since their completion and operation.

Title V Operating Permit Program

44. As alleged in Paragraphs 34 through 43, Lehigh commenced one or more major modifications at its Facility commencing from 1996 through 1999, and the modifications triggered the requirements to obtain a PSD permit, undergo a PSD BACT analysis, and operate in compliance with the PSD permit. Lehigh failed to satisfy these requirements.

45. Lehigh first submitted a Title V application to BAAQMD on June 21, 1996. The final permit was issued by BAAQMD on November 5, 2003.

46. Prior to issuance of the Title V permit, Lehigh failed to supplement and/or correct its Title V permit application to identify all applicable requirements, including PSD requirements for NO_x and SO_2, a plan to come into compliance with those PSD requirements, and an updated certification of compliance that included the PSD requirements.

47. As a result of Lehigh's failure to provide complete information in its application or to supplement and/or correct

its application to include PSD requirements, Lehigh obtained a deficient Title V operating permit that did not contain all applicable requirements.

48. Pursuant to Section 502(a) of the CAA, 42 U.S.C. § 7661a(a), it is unlawful for any person to operate a source required to have a PSD permit except in compliance with a permit issued by a permitting authority under Title V. Similarly, 40 C.F.R. §§ 70.1(b), 70.6(a) and BAAQMD Rule 2-6-409 require sources subject to Title V to have an operating permit that assures compliance with all applicable requirements.

49. Lehigh has operated and continues to operate the Facility without a valid Title V operating permit in violation of Sections 502, 503 and 504 of the Act, 42 U.S.C. §§ 7661a, 7661b, and 7661c; 40 C.F.R. §§ 70.1, 70.5 and 70.6; and BAAQMD Regulation 2 Rule 6.

FINDING OF VIOLATION

Prevention of Significant Deterioration

50. Pursuant to Section 113(a)(1) of the Act, notice is hereby given to Lehigh that the Administrator of the EPA, by authority duly delegated to the undersigned, finds that Lehigh is in violation of federal PSD requirements at the Facility described in this NOV/FOV. EPA reserves the right to amend this NOV/FOV or issue a new NOV/FOV based on additional information obtained through Section 114 of the Act or any other source available to the Administrator at any point.

Title V Operating Permit Program

51. Notice is also given to Lehigh that it failed to supplement or correct its Title V application submitted to BAAQMD to include PSD requirements or obtain a Title V permit that contained PSD requirements, and therefore is in violation of Title V of the Act.

ENFORCEMENT

52. For any violation of a SIP, such as for PSD violations, Section 113(a)(1) of the Act, 42 U.S.C. § 7413(a)(1), provides that at any time after the expiration of 30 days following the date of the issuance of a notice of violation, the Administrator may, without regard to the period of violation, issue an order requiring compliance with the requirements of the SIP, issue an administrative penalty order, or bring a civil action pursuant to Section 113(b) for injunctive relief and/or civil penalties of not more than $25,000 per day for each violation that occurs on or before January 30, 1997, not more than $27,500 per day for each violation that occurs after January 30, 1997, not more than $32,500 per day for each violation that occurs after March 14, 2004; and not more than $37,500 per day for each violation that occurs after January 12, 2009. 42 U.S.C. § 7413(a)(1); Federal Civil Penalties Inflation Adjustment Act of 1990, Pub. L. 101-410, as amended; 40 C.F.R. Part 19.

53. Sections 113(a)(3) and 167 of the Act, 42 U.S.C. §§ 7413(a)(3) and 7477, provide additional authority for EPA to enforce against violators of the Act.

54. Section 113(c) of the Act, 42 U.S.C. § 7413(c), provides for criminal penalties, imprisonment, or both for persons who knowingly violate any federal regulation or permit requirement. For violations of the SIP, a criminal action can be brought 30 days after the date of issuance of a Notice of Violation.

55. Section 306 of the Act, 42 U.S.C. § 7606, the regulations promulgated thereunder (2 C.F.R. Part 180), and Executive Order 11738 provide that facilities to be utilized in federal contracts, grants and loans must be in full compliance with the Act and all regulations promulgated pursuant to it. A violation of the Act may result in Lehigh and/or the Facility being declared ineligible for participation in any federal contract, grant, or loan.

PENALTY ASSESSMENT CRITERIA

56. Section 113(e)(1) of the Act, 42 U.S.C. § 9613(e)(1), states that the Administrator or the court shall determine the amount of a penalty to be assessed by taking into consideration such factors as justice may require, including the size of the business, the economic impact of the penalty on the business, the violator's full compliance history and good faith efforts to comply, the duration of the violation as established by any credible evidence (including evidence other than the applicable test method), payment by the violator of penalties previously assessed for the same violations, the economic benefit of noncompliance, and the seriousness of the violation.

57. Section 113(e)(2) of the Act, 42 U.S.C. § 9613(e)(2),

allows the Administrator or the court to assess a penalty for each day of violation. This section further provides that for purposes of determining the number of days of violation, where EPA makes a prima facie showing that the conduct or events giving rise to the violation are likely to have continued or recurred past the date of an NOV, the days of violation shall be presumed to include the date of the NOV and each and every day thereafter until the facility establishes that continuous compliance has been achieved, except to the extent that the facility can prove by the preponderance of the evidence that there were intervening days during which no violation occurred or that the violation was not continuing in nature.

OPPORTUNITY FOR CONFERENCE

58. Lehigh may confer with EPA regarding this NOV/FOV if it so requests. A conference would enable Lehigh to present evidence bearing on the finding of violation, on the nature of violation, and on any efforts it may have taken or proposes to take to achieve compliance. If Lehigh seeks such a conference, it may choose to be represented by counsel. If Lehigh wishes to confer with EPA, it must make a request for a conference within 10 working days of receipt of this NOV/FOV. Any request for a conference or other inquiries concerning the NOV/FOV should be made in writing to:

Ivan Lieben
Office of Regional Counsel
U.S. EPA (ORC-2)
75 Hawthorne Street
San Francisco, CA 94105

(415)972-3914

Dated: 3-9-10

Deborah Jordan
Director, Air Division

EXHIBIT 11

Linda S. Adams
Agency Secretary

California Regional Water Quality Control Board
San Francisco Bay Region

1515 Clay Street, Suite 1400, Oakland, California 94612
(510) 622-2300 • Fax (510) 622-2460
http://www.waterboards.ca.gov/sanfranciscobay

Arnold Schwarzenegger
Governor

Sent via certified Mail - Return Receipt Requested

March 26, 2010

Lehigh Southwest Cement Co.
c/o Scott Renfew, Environmental Manager
24001 Stevens Creek Boulevard
Cupertino , CA 95014

Subject: **NOTICE OF VIOLATION and required corrective actions for failure to protect stormwater at industrial facility**

Facility: **Lehigh Southwest Cement Co. (formally Hanson Permanente Cement) Industrial facility, located at 24001 Stevens Creek Boulevard, Cupertino, Santa Clara County WDID No. 2 43I006267**

Dear Mr. Renfew:

You are hereby given notice that the industrial facility indicated above (Facility) is in violation of stormwater protection requirements. On behalf of Water Board staff, a PG Environmental, LLC, inspector recently inspected the Facility, and noted numerous water quality violations. **You are required to correct the problems noted in the attached Inspection Findings, Violations, and Corrective Actions Report and send us documentation of your corrective actions by the dates indicated in this Report.**

The Facility is in violation of the NPDES General Permit for Discharges of Storm Water associated with Industrial Activities Excluding Construction Activities, Order No. 97-03-DWQ (Permit[1]) and the San Francisco Bay Water Quality Control Plan (Basin Plan[2]).

Permit violations
The Permit requires industrial facility owners to implement controls that reduce pollutants in stormwater discharges to the Best Available Technology Economically Achievable/Best Conventional Pollutant Control Technology (BAT/BCT) performance standard. Development and implementation of a Storm Water Pollution Prevention Plan that complies with the requirements in Section A of the Permit and that includes Best Management Practices (BMPs)

[1] Permit: http://www.waterboards.ca.gov/water_issues/programs/stormwater/industrial.shtml
[2] Basin Plan Table 4.1, Prohibitions: http://www.waterboards.ca.gov/sanfranciscobay/water_issues/programs/planningtmdls/basinplan/web/tab/tab_4-01.pdf

that achieve BAT/BCT constitutes compliance with this requirement. Our inspector observed that the Facility does not meet this standard, and therefore, the Facility is in violation of the Permit.

Basin Plan Prohibition violations
Additionally, the Facility is in violation of the Basin Plan, which is the Regional Water Board's master water quality control document. The Basin Plan applies to all discharges within the Regional Water Board's jurisdiction, including discharges from this Facility. We observed during the February 10, 2010, inspection evidence of discharges that are in violation of, at a minimum, Basin Plan Prohibition 7:

- **Prohibition 7** prohibits rubbish, refuse, bark, sawdust, or other solid wastes into surface waters or at any place where they would contact or where they would be eventually transported to surface waters, including flood plain areas.

Please refer to the attached inspection report for the details of the violations and required corrective actions.

Consequences for not coming into compliance
Failure to return to compliance with the Permit and failure to comply with the Basin Plan prohibitions are violations of CWC Section 13385(a)(2) and (a)(4), respectively, for which the Water Board may impose civil liability in the amount not to exceed $10,000 per day of each violation, plus $10 per gallon in excess of 1,000 gallons per discharge.

Additional notes
If you need guidance, the California Stormwater Quality Association (CASQA) publishes a handbook for Industrial Stormwater Best Management Practices[3]. The CASQA handbook is one of many online resources that describe industry standard BMPs. Please note that Water Board can not specify means of compliance. It is your responsibility to select and correctly implement an appropriate suite of BMPs. Use of the CASQA handbook or other similar guidance documents may help you achieve compliance, but it does not guarantee compliance.

If you have any questions regarding this letter, please contact Christine Boschen at (510) 622-2346 or by email at cboschen@waterboards.ca.gov.

Sincerely,

Dyan C. Whyte

Dyan C. Whyte
Assistant Executive Officer

Encl.: February 10, 2010, Inspection Findings, Violations, and Corrective Actions

[3] CASQA BMP Handbook: http://www.cabmphandbooks.com/Industrial.asp

February 10, 2010, Inspection Photo Log
February 10, 2010, Inspection Exhibit Log

cc:

Stuart Tomlinson, VP
Lehigh Southwest Cement Co.
12667 Alcosta Boulevard, Suite 400
San Ramon, CA 94583

Jeff Brummert, VP
Lehigh Southwest Cement Co.
12667 Alcosta Boulevard, Suite 400
San Ramon, CA 94583

David W. Knapp, City Manager
City of Cupertino
By e-mail dknapp@cupertino.org

Rick Kitson, Director
Public and Environmental Affairs
City of Cupertino
By e-mail rickk@cupertino.org

Timothy Stevens
Department of Fish and Game
By e-mail tstevens@dfg.ca.gov

Thu Bui
Air Resources Control Board
By e-mail tbui@baaqmd.gov

Rebecca Glyn
USEPA
By e-mail glyn.rebecca@epa.gov

Ann Murphy
USEPA
Murphy.ann@epamail.epa.gov

Cathy Helgerson
2020697 Dunbar Drive
Cupertino, CA 95-14

Trish Mulvey
By e-mail mulvey@ix.netcom.com

Amy Chastain
BayKeeper
amy@baykeeper.org

Scott Coulson
PG Environmental
By e-mail scott.coulson@pgenv.com

Brenner Perryman
PG Environmental
By e-mail
Brenner.perryman@pgenv.com

EXHIBIT 12

California Regional Water Quality Control Board
San Francisco Bay Region

Linda S. Adams
Secretary for
Environmental Protection

1515 Clay Street, Suite 1400, Oakland, California 94612
(510) 622-2300 • Fax (510) 622-2460
http://www.waterboards.ca.gov/sanfranciscobay

Arnold Schwarzenegger
Governor

Sent via certified Mail - Return Receipt Requested

Date: November 29, 2010

Lehigh Southwest Cement Co.
c/o Mr. Henrik Wesseling
24001 Stevens Creek Boulevard
Cupertino CA 95014

SUBJECT: **Requirement for Technical Report to Document Non-Storm Water Discharge(s) Pursuant to California Water Code Section 13267**

Facility: Lehigh Southwest Cement Company (formally Hanson Permanente Cement) Industrial Facility, Located at
24001 Stevens Creek Boulevard,
Cupertino, Santa Clara County
WDID No. 2 43I006267

Dear Mr. Wesseling:

This Order requires Lehigh Southwest Cement Co. ("Lehigh") to submit a technical report, by January 7, 2011, containing the following information and analyses:

- A characterization of any and all non-stormwater discharge(s) that occurred during (but possibly not limited to) mid-to-late September, 2010; and
- A description of any and all non-stormwater discharges to Permanente Creek from the Lehigh facility and/or resulting from Lehigh's operations at the facility during the past three years.

This Order is issued by the San Francisco Bay Water Board pursuant to its authority under Water Code section 13267. Your failure to comply with this Order could subject you misdemeanor charges and/or subject you to civil liability as provided for in Water Code section 13268.

Background

On September 15, 2010, the Santa Clara Valley Water District (SCVWD) received a telephone call from a local resident claiming to have observed increased stream flows in Permanente Creek in the vicinity of Portland Drive and Miramonte Avenue in Los Altos. SCVWD notified us of the discharge. We then contacted Scott Renfrew, Lehigh Environmental Compliance Manager, by telephone on October 4, 2010, to ask about the discharge. During that conversation, Mr. Renfrew

explained that the Lehigh facility was pumping water from the quarry bottom, routing the water through Pond #4, and discharging the water into Permanente Creek. Mr. Renfrew further explained that the discharge to Permanente Creek is a routine maintenance activity conducted during the summer months.

Specific Requirements of This Order

You are required to submit a technical report no later than January 7, 2011, containing the all information described herein. The report must document the nature, volume, and duration of the discharge noted above, and the nature, volume, and duration of any and all other similar discharges that have occurred in the past three years or that are currently ongoing from the Lehigh facility. Specifically, you are required to provide the following information:

1. Regarding the discharge(s) from Pond #4 that occurred in September 2010:

a) The specific time period of the discharge (total number of hours including start and end time).

b) The total number of gallons discharged.

c) A map showing, at a minimum, the locations of the source of discharged water, likely flow paths, associated structures and piping, pumping and treatment controls, and all discharge points into Permanente Creek. Any other records necessary to document the location and manner of the discharge must be included. The map must clarify whether the water discharged was into an in-stream pond constructed within Permanente Creek.

d) Detailed aerial and ground level photographs and as-built drawings showing the features listed above in (c).

e) A detailed description of the methods used to monitor and observe the discharge.

f) All available records pertaining to the discharge, such as and including those for inspections, maintenance, flow rate monitoring, pollutant monitoring. All records must be dated. Documents such as inspector's field notes, visual monitoring data, sampling data, laboratory analytical data, continuous and/or automated monitoring data, if they exist, must be included. If they do not exist, you must submit a statement to that effect under penalty of perjury.

g) Prior to sampling and no later than December 13, 2010, Lehigh shall propose a sampling plan aimed at characterizing the quality of water discharged on September 15, 2010. The plan must address any variability in the discharged waters and justify sample locations and sampling methods. The samples must be analyzed for the full California Toxics rule (CTR) constituent list (Attachment B), and additional constituents common to discharges from aggregate mining facilities (Attachment C).

2) **Regarding all other non-stormwater discharges that occurred in the last 3 years:** Provide all information as described above.

This requirement for a report is made pursuant to California Water Code Section 13267, which allows the Regional Water Board to require technical or monitoring program reports from any person who has discharged, discharges, proposes to discharge, or is suspected of discharging waste that could affect water quality. Under Section 13267 of the Water Code, Lehigh must furnish such required technical reports under penalty of perjury. Attachment D provides additional information about Section 13267 requirements. Failure or refusal to submit this technical report, and/or submittal of falsified information, may subject you to a misdemeanor and/or up to $5,000 per day of violation in civil liabilities, while submittal of late or inadequate reports may result in the imposition of civil liability of up to $5,000 per day of violation per Section 13268 of the Water Code.

If you have any questions, please contact Cecilio Felix of my staff at (510) 622-2343, or by e-mail at cfelix@waterboards.ca.gov.

Sincerely,

Dyan C. Whyte

Dyan C. Whyte
Assistant Executive Officer

Attachments

A. Mailing List
B. California Toxics Rule (CTR) constituent list
C. Additional Constituents Common to Discharge from Aggregate Mining Facilities
D. Fact Sheet: Requirements for Submitting Technical Reports under Section 13267 of the California Water Code

EXHIBIT 13

County of Santa Clara

Department of Planning and Development
Administration

County Government Center, East Wing, 7th Floor
70 West Hedding Street
San Jose, California 95110-1705
(408) 299-6740 FAX (408) 288-9198

October 10, 2006

John Giovanola
Hanson Permanente Cement, Inc.
24001 Stevens Creek Road
Cupertino, CA 95014

ORDER TO COMPLY/NOTICE OF VIOLATION
(Pub. Res. Code § 2774.1)

Dear Mr. Giovanola:

On September 22, 2006, the Department of Conservation's Office of Mine Reclamation (OMR) issued a "15-Day Notice" to the County of Santa Clara pursuant to Public Resources Code § 2774.1 (f)(1). The 15-Day Notice alleged several SMARA violations at Hanson Permanente Cement, Inc.'s (Hanson's) Permanente Quarry. Pursuant to § 2774.1(f), if the County does not take appropriate enforcement action in response to this notice, OMR may initiate enforcement.

Accordingly, the County hereby issues a Notice of Violation (NOV) and Order to Comply to Hanson's Permanente Quarry for mining-related disturbance outside the approved reclamation plan with the exception of the cement plant. At this time, the County is not requiring Hanson to include the adjacent cement plant site within the amended reclamation plan boundaries. As you know, the cement plant is a separately permitted and vested industrial facility which pre-dates SMARA by nearly 40 years and the County expressly excluded the cement plant from the approved reclamation plan in 1985. To date, the County has also been unable to find any clear guidance in the law or regulation regarding whether, under these circumstances, SMARA requires the cement plant to be included in the reclamation plan. Please note, however, that OMR may decide to take enforcement action on this issue. If this issue ultimately reaches the State Mining and Geology Board (SMGB), the County will adhere to the SMGB's decision on this issue.

File 2250

The issues addressed in this NOV have already been the subject of numerous discussions between the County and Hanson. As a result of these meetings, Hanson at this time has agreed to file an amended reclamation plan encompassing all disturbed areas (except the cement plant and former aluminum plant sites) and to comply with the County's compliance schedule (attached). The amended reclamation plan will address, among other things, the slope instability along the north wall of the pit, and encompass all mining-related access roads, structures, stockpiles and storage areas, including the rock processing facility to the south of the cement plant. The amendment will also calculate, for posting on an interim basis pending final reclamation plan approval, new financial assurances. Hanson at this time has also agreed to waive the hearing requirement in Public Resources Code § 2774.1(b). Please confirm that this accurately represents Hanson's position.

We appreciate Hanson's cooperative attitude in this matter and express the County's commitment to work diligently with Hanson to expeditiously resolve all outstanding issues.

Sincerely,

Val Alexeeff
Director of Planning

cc: Douglas W. Craig, Assistant Director, OMR
Allen M. Jones, Chair, SMGB
Stephen M. Testa, Executive Officer, SMGB
Pete Kutras, County Executive, Santa Clara County
Jane Decker, Deputy County Executive, Santa Clara County
Ann Ravel, County Counsel, Santa Clara County
Lizanne Reynolds, County Counsel, Santa Clara County

COMPLIANCE SCHEDULE – HANSON PERMANENTE

Deadline	Action
11/15/06-11/30/06	Pre-application meeting between County Planning Department and Hanson concerning reclamation plan amendment.
12/15/06-12/31/06	Hanson to submit an application for an amended reclamation plan, and interim financial assurance calculations.
1/15/07-1/31/07	The County to complete its 30-day review of the application, and inform Hanson in writing whether the application is complete for processing or additional information is required.
No later than 3/16/07	Hanson to resubmit a revised application containing additional information required by the 30-day review letter.
4/16/07	The County to inform Hanson that the application is complete for processing. The County to provide approval for interim financial assurances, for immediate posting. The County to forward the amended reclamation plan and financial assurances to OMR for comments pursuant to Public Resources Code section 2774, subdivision (c).
4/20/07	The County to begin processing and CEQA review of the amended reclamation plan.
5/15/07	OMR to provide any comments regarding the amended reclamation plan, pursuant to the 30-day review period of Public Resources Code section 2774, subdivision (d)(1).
6/1/07	OMR to provide any comments regarding the updated financial assurances, pursuant to the 45-day review period of Public Resources Code section 2774, subdivision (d)(1).
7/20/07-8/17/07	The County to complete the CEQA review. Based on assumption that the document will be a Mitigated Negative Declaration and that public participation will not be unusually strong.
8/20/07	Public release of the proposed CEQA environmental document and beginning of the public comment period.

10/8/07	Close of CEQA public comment period.
10/15/07	Prepare early response to OMR of public hearing on amended reclamation plan and revised financial assurances, pursuant to SB 668.
11/15/07	County to prepare staff report concerning application for amended reclamation plan and financial assurances.
11/30/07-12/30/07	Public hearing on application for amended reclamation plan and financial assurances.

EXHIBIT 14

County of Santa Clara

Department of Planning and Development
Planning Office

County Government Center, East Wing, 7th Floor
70 West Hedding Street
San Jose, California 95110-1705
(408) 299-5770 FAX (408) 288-9198
www.sccplanning.org

June 20, 2008

Marvin E. Howell
Hanson Aggregates West, Inc.
P.O. Box 639069
San Diego CA 92163-9069

John Giovanola
Hanson Permanente Cement
24001 Stevens Creek Blvd
Cupertino CA 95014-5659

Subject: NOTICE OF VIOLATION (PRC §2774.1)

Dear Mr. Howell and Mr. Giovanola:

On April 3, 2008, the County of Santa Clara received a complaint alleging Hanson Permanente Quarry was storing stockpiles of petroleum coke on land owned and operated by the quarry. Subsequently, staff from the County Planning Office met with Hanson personnel in the field on April 8, 2008, to locate the stockpiled material in the field. Following this field inspection staff also met with the County Geologist and a consultant from the geology firm retained by the Planning Office to assist with the 2007 SMARA inspection of Hanson Permanente. Based on this field review and subsequent discussion with the County Geologist and consultant, both of who participated in the most recent SMARA inspection, the County has determined the following:

1. The material shown in the photographs included with the complaint is not petroleum coke.
2. The material is stockpiled overburden from the mine.
3. The location where the stockpiled materials were found is within an area included in the boundary of a proposed reclamation plan amendment, but is not located within the boundary of the current, approved reclamation plan boundary.

The County of Santa Clara previously issued a combined Order to Comply/Notice of Violation (NOV) to Hanson on October 10, 2006, for having areas of disturbance outside the approved reclamation plan boundary. Hanson subsequently applied for a reclamation plan amendment to address this issue. The NOV effectively placed Hanson on notice that work outside the reclamation plan boundary is not authorized. For this reason, the County views this additional stockpiling as an intensification of an existing violation.

In keeping with the requirements of SMARA §2774.1, the County hereby issues a Notice of Violation for mining related disturbance outside the approved reclamation plan, and specifically for stockpiling in an area east of the approved reclamation plan.

Because the approved reclamation plan provides for an area to receive overburden in the portion of the mined land identified as "Area A," which has space available to receive such material, you are hereby required to accomplish the following:

(1) cease depositing the material in the location described above, and

(2) submit a proposal for either

(a) removing the material, or

(b) providing for interim erosion control and re-vegetation of the stockpile in order to retain the material while the reclamation plan amendment continues to be processed.

The County Planning Office must receive the abatement proposal, identified in item #2 above, on or before July 21, 2008.

If you have any questions regarding this matter please contact me via email at Gary.Rudholm@pln.sccgov.org, or by telephone at (408) 299-5747.

Sincerely,

Gary Rudholm

Gary Rudholm
Senior Planner

cc: Cy Oggins, State Office of Mine Reclamation
Stephen Testa, Executive Officer, State Mining & Geology Board
Jody Hall Esser, Interim Director of Planning & Development
Michael M. Lopez, Planning Manager
Lizanne Reynolds, Deputy County Counsel

EXHIBIT 15

CLAYTON & McEVOY
A Professional Corporation
333 West Santa Clara Street, Suite 950
San Jose, California 95113-1721

William B. Clayton, Jr.
Laurence J. McEvoy
Henry W. Roux
Joshua A. Bennett

Telephone: (408) 293-9100
Facsimile: (408) 293-4172
jab@clayton-mcevoy.com

www.clayton-mcevoy.com

October 14, 2010

Via U.S. First Class Mail

Lehigh Southwest Cement Company
Attn: Henrik Wesseling, Plant Manager
Lehigh Southwest Cement Company
24001 Stevens Creek Boulevard
Cupertino, CA 95014-5659

Lehigh Southwest Cement Company
Corporate Headquarters
Attn: Current CEO or President
Lehigh Hanson, Inc.
300 E. John Carpenter Freeway
Irving, TX 75062

CSC - LAWYERS INCORPORATING SERVICE
C/o: Lehigh Southwest Cement Company
Attn: Henrik Wesseling, Plant Manager or current CEO or President
2730 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833

Re: *Notice of Violation of the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65), Section 25249.6 of the California Health and Safety Code, for Exposing Individuals Present and Residing in Santa Clara County, California, to Arsenic, Benzene and Chromium 6, in the course of producing Type II/V (Low-Alkali), Type III (Hi-Early Strength), Slag Cement, Type I-P, APPC, and TioCem Cements.*

Dear Sir/Madam:

Quarry No is an association of residents residing in Santa Clara County, California, and dedicated to the preservation and enhancement of human health and the environment. Quarry No has a long-standing interest in reducing health hazards to the public posed by toxic chemicals and protecting the public from harmful substances.

Quarry No and Mr. William J. Almon, acting individually and as Quarry No's representative, hereby give you notice that the Lehigh Southwest Cement Company (hereinafter "Lehigh"), doing business at 24001 Stevens Creek Boulevard, Cupertino, CA 95014-5659, has violated and continues to violate provisions of the Safe Drinking Water and Toxic Enforcement Act of 1986, California Health and Safety Code §§ 25249.5 et seq. Specifically, that Lehigh has violated and continue to violate the warning

requirement of § 25249.6 of the California Health and Safety Code, which provides, "No person in the course of doing business shall knowingly and intentionally expose any individual to a chemical known to the state to cause cancer or reproductive toxicity without first giving clear and reasonable warning to such individual..."

Lehigh's production and sale of Type II/V (Low-Alkali), Type III (Hi-Early Strength), Slag Cement, Type I-P, APPC, and TioCem Cements, among others, has exposed and continues to expose individuals present and residing in Santa Clara, County, California, including Mr. Almon, to harmful levels of Arsenic, Benzene and Chromium 6, through their inhalation, dermal absorption and other bodily contact via Lehigh's industrial processes. These chemicals are known by the State of California to cause reproductive toxicity and cancer.

Because Arsenic, Benzene and Chromium 6 are chemicals listed in Proposition 65 as human carcinogens and reproductive toxins, pursuant to Health and Safety Code § 25249.6, Lehigh was, and is, required to provide clear and reasonable warnings before knowingly and intentionally exposing any individual to those substances in the course of its business. Since June 1, 2007, to the present, Lehigh has exposed and continues to expose individuals present and residing in Santa Clara, County, California, to harmful levels of Arsenic, Benzene and Chromium 6, through its daily industrial processes and without a clear and reasonable warning as required under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65), § 25249.6 of the California Health and Safety Code. These violations will continue to occur until Lehigh provides adequate warnings.

Therefore, pursuant to Health and Safety Code § 25249.7(d), Quarry No and Mr. William J. Almon intend to bring suit in the public interest against Lehigh sixty (60) days hereafter to correct the violation occasioned by Lehigh's failure to warn all those individuals exposed in Santa Clara County, California, to its harmful levels of Arsenic, Benzene and Chromium 6.

Pursuant to 27 California Code of Regulations § 25903(b)(1), attached hereto as Exhibit "1" is a copy of "The Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): A Summary," a summary of Proposition 65 prepared by the Office of Environmental Health Hazard Assessment of the California Environmental Protection Agency.

Pursuant to Health and Safety Code § 25249.7(d)(1), the undersigned hereby includes with the copy of this Notice to the California Attorney General a confidential Certificate of Merit. Pursuant to 27 California Code of Regulations § 25903(c)(3), the noticing parties are providing this Notice to the California Attorney General, the District Attorney of Santa Clara County and the City Attorneys of the cities of Los Altos, Los Altos Hills, Cupertino, Mountain View and Sunnyvale as evidenced in Exhibit "2" attached hereto.

The noticing parties are represented by Clayton & McEvoy, P.C. All communications concerning this matter should please be directed to:

Joshua A. Bennett
Clayton & McEvoy, P.C.
333 W. Santa Clara St. #950
San Jose, CA 95113-1717

333 W. Santa Clara St. #950
San Jose, CA 95113-1717
Email: jab@clayton-mcevoy.com
Telephone: (408) 293-9100

Very truly yours,

CLAYTON & McEVOY, P.C.

Joshua A. Bennett
JAB/lc

Enclosures
cc: Attorney General of California (Confidential factual information supporting Certificate of Merit attached)
District Attorney of Santa Clara County, California
City Attorney of Los Altos Hills, California
City Attorney of Los Altos, California
City Attorney of Cupertino, California
City Attorney of Sunnyvale, California
City Attorney of Mountain View, California

(See attached Certificate of Service)

EXHIBIT "1"

OFFICE OF ENVIRONMENTAL HEALTH
HAZARD ASSESSMENT
CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

THE SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986 (PROPOSITION 65): A SUMMARY

The following summary has been prepared by the Office of Environmental Health Hazard Assessment, the lead agency for the implementation of the Safe Drinking Water and Toxic Enforcement Act of 1986 (commonly known as "Proposition 65"). A copy of this summary must be included as an attachment to any notice of violation served upon an alleged violator of the Act. The summary provides basic information about the provisions of the law, and is intended to serve only as a convenient source of general information. It is not intended to provide authoritative guidance on the meaning or application of the law. The reader is directed to the statute and its implementing regulations (see citations below) for further information.

Proposition 65 appears in California law as Health and Safety Code Sections 25249.5 through 25249.13. Regulations that provide more specific guidance on compliance, and that specify procedures to be followed by the State in carrying out certain aspects of the law, are found in Title 22 of the California Code of Regulations, Sections 12000 through 14000.

WHAT DOES PROPOSITION 65 REQUIRE?

The "Governor's List." Proposition 65 requires the Governor to publish a list of chemicals that are known to the State of California to cause cancer, or birth defects or other reproductive harm. This list must be updated at least once a year. Over 735 chemical listings have been included as of November 16, 2001. Only those chemicals that are on the list are regulated under this law. Businesses that produce, use, release or otherwise engage in activities involving those chemicals must comply with the following:

Clear and reasonable warnings. A business is required to warn a person before "knowingly and intentionally" exposing that person to a listed chemical. The warning given must be "clear and reasonable." This means that the warning must: (1) clearly make known that the chemical involved is known to cause cancer, or birth defects or other reproductive harm; and (2) be given in such a way that it will effectively reach the person before he or she is exposed. Exposures are exempt from the warning requirement if they occur less than twelve months after the date of listing of the chemical.

Prohibition from discharges into drinking water. A business must not knowingly discharge or release a listed chemical into water or onto land where it passes or probably will pass into a source of drinking water. Discharges are exempt from this requirement if they occur less than twenty months after the date of listing of the chemical.

DOES PROPOSITION 65 PROVIDE ANY EXEMPTIONS?

Yes. The law exempts: Governmental agencies and public water utilities. All agencies of the federal, State or local government, as well as entities operating public water systems, are exempt.

Businesses with nine or fewer employees. Neither the warning requirement nor the discharge prohibition applies to a business that employs a total of nine or fewer employees. Exposures that pose no significant risk of cancer. For chemicals that are listed as known to the State to cause cancer ("carcinogens"), a warning is not required if the business can demonstrate that the exposure occurs at a level that poses "no significant risk." This means that the exposure is calculated to result in not more than one excess case of cancer in 100,000 individuals exposed over a 70-year lifetime. The Proposition 65 regulations identify specific "no significant risk" levels for more than 250 listed carcinogens.

Exposures that will produce no observable reproductive effect at 1,000 times the level in question. For chemicals known to the State to cause birth defects or other reproductive harm ("reproductive toxicants"), a warning is not required if the business can demonstrate that the exposure will produce no observable effect, even at 1,000 times the level in question. In other words, the level of exposure must be below the "no observable effect level (NOEL)," divided by a 1,000-fold safety or uncertainty factor. The "no observable effect level" is the highest dose level which has not been associated with an observable adverse reproductive or developmental effect.

Discharges that do not result in a "significant amount" of the listed chemical entering into any source of drinking water. The prohibition from discharges into drinking water does not apply if the discharger is able to demonstrate that a "significant amount" of the listed chemical has not, does not, or will not enter any drinking water source, and that the discharge complies with all other applicable laws, regulations, permits, requirements, or orders. A "significant amount" means any detectable amount, except an amount that would meet the "no significant risk" or "no observable effect" test if an individual were exposed to such an amount in drinking water.

HOW IS PROPOSITION 65 ENFORCED?

Enforcement is carried out through civil lawsuits. These lawsuits may be brought by the Attorney General, any district attorney, or certain city attorneys (those in cities with a population exceeding 750,000). Lawsuits may also be brought by private parties acting in the public interest, but only after providing notice of the alleged violation to the Attorney General, the appropriate district attorney and city attorney, and the business accused of the violation. The notice must provide adequate information to allow the recipient to assess the nature of the alleged violation. A notice must comply with the information and procedural requirements specified in regulations (Title 22, California Code of Regulations, Section 25903). A private party may not pursue an enforcement action directly under Proposition 65 if one of the governmental officials noted above initiates an action within sixty days of the notice.

A business found to be in violation of Proposition 65 is subject to civil penalties of up to $2,500 per day for each violation. In addition, the business may be ordered by a court of law to stop committing the violation.

FOR FURTHER INFORMATION. . .

Contact the Office of Environmental Health Hazard Assessment's Proposition 65 Implementation Office at (916) 445-6900.

EXHIBIT "2"

Attorney General Edmund G. Brown, Jr. California Attorney General's Office 1300 "I" Street P.O. Box 944255 Sacramento, CA 94244-2550 (With confidential factual information supporting the Certificate of Merit Included)	Santa Clara County, California District Attorney Dolores Carr 70 W. Hedding Street, West Wing San Jose, CA 95110
City of Los Altos Hills, California City Attorney Steven Mattas Town Hall Offices 26379 Fremont Road Los Altos Hills, CA 94022	City of Los Altos, California City Attorney One North San Antonio Road Los Altos, CA 94022
City of Cupertino, California City Attorney Carol Korade 20410 Town Center Lane #210 Cupertino, CA 95014-3220	City of Sunnyvale, California City Attorney David Kahn 456 W. Olive Ave. Sunnyvale, CA 94086
City of Mountain View, California City Attorney Jannie Quinn 500 Castro Street Mountain View, CA 94039-7540	

CERTIFICATE OF MERIT
[California Health & Safety Code § 25249.7(d)]

I, Joshua A. Bennett, hereby declare:

1. This Certificate of Merit accompanies the attached notice of violation in which it is alleged that the parties identified in the notice have violated California Health & Safety Code § 25249.6, by failing to provide clear and reasonable warnings.

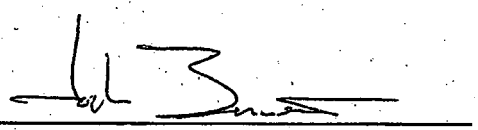
2. I am an attorney representing the Noticing Parties, Quarry No and Mr. William J. Almon.

3. I have consulted with one or more persons with relevant and appropriate experience or expertise who has reviewed facts, studies, or other data regarding the alleged exposure to the listed chemicals that are the subject of the action.

4. Based upon the information obtained through those consultations, and on all other information in my possession, I believe there is a reasonable and meritorious case for the underlying private action. I understand that "reasonable and meritorious case for the private action" means that the information provides a credible basis that all elements of the Plaintiffs' case can be established and the information did not prove that the alleged violator will be able to establish any of the affirmative defenses set forth in the statute.

5. The copy of this Certificate of Merit served upon the California Attorney General attaches to it factual information sufficient to establish the basis for this Certificate, including the information identified in California Health & Safety Code § 25249.7(h)(2), i.e., (1) the identity of the persons consulted with and relied on by the Certifier, and (2) the facts, studies, or other data reviewed by those persons.

Date: October 14, 2010



Joshua A. Bennett
Attorney for Noticing Parties, Quarry No
and Mr. William J. Almon

CERTIFICATE OF SERVICE
STATE OF CALIFORNIA, COUNTY OF SANTA CLARA

I, Linda Childers, hereby declare:

I am a citizen of the United States, over 18 years of age, and not a party to the within action. I am employed in the County of Santa Clara; my business address is 333 W. Santa Clara St., Suite 950, San Jose, CA 95113.

On October 15, 2010, I served the within:

Notice of Violation of the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65), Section 25249.6 of the California Health and Safety Code, for Exposing Individuals Present and Residing in Santa Clara County, California, to Arsenic, Benzene and Chromium 6, in the course of producing Type II/V (Low-Alkali), Type III (Hi-Early Strength), Slag Cement, Type I-P, APPC, and TioCem Cements;

Proposition 65: A Summary;

Certificate of Merit;

Certificate of Merit Attachments (Served only on the California Attorney General).

on all parties in this action, as addressed below, by causing a true copy thereof to be distributed as follows: *See Attachment 1 – Service List.*

☑ **BY MAIL:** I am "readily familiar" with the firm's practice of collection and processing correspondence for mailing. Under that practice it would be deposited with the U.S. Postal Service on that same day with postage thereon fully prepaid in the ordinary course of business. I am aware that on motion of the party served, service is presumed invalid if the postal cancellation date or postage meter date is more than one day after date of deposit for mailing an affidavit.

☐ **BY HAND DELIVERY:** I caused such documents to be hand delivered to the stated parties.

☐ **VIA TELEFACSIMILE:** I caused such documents to be transmitted via telefacsimile to the stated parties at their respective facsimile numbers. The facsimile transmission(s) was reported as complete and without error and said transmission report(s) is attached to this proof of service.

☐ **VIA FEDERAL EXPRESS:** I caused such documents to be collected by an agent for Federal Express to be delivered to the offices of the stated parties, next day service/Saturday delivery requested.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Dated: October 15, 2010

Linda Childers

Linda Childers

Attachment 1 – Service List

Lehigh Southwest Cement Company
Attn: Henrik Wesseling, Plant Manager
Lehigh Southwest Cement Company
24001 Stevens Creek Boulevard
Cupertino, CA 95014-5659

Lehigh Southwest Cement Company
Corporate Headquarters
Attn: Current CEO or President
Lehigh Hanson, Inc.
300 E. John Carpenter Freeway
Irving, TX 75062

CSC - LAWYERS INCORPORATING SERVICE
c/o: Lehigh Southwest Cement Company
Attn: Henrik Wesseling, Plant Manager or current CEO or President
2730 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833

Attorney General Edmund G. Brown, Jr.
Attorney General's Office
1300 "I" Street
P.O. Box 944255
Sacramento, CA 94244-2550

(With confidential factual information supporting the Certificate of Merit Included)

Santa Clara County, California
District Attorney Dolores Carr
70 W. Hedding Street, West Wing
San Jose, CA 95110

City of Los Altos Hills, California
City Attorney Steven Mattas
Town Hall Offices
26379 Fremont Road
Los Altos Hills, CA 94022

City of Los Altos, California
City Attorney
One North San Antonio Road
Los Altos, CA 94022

City of Cupertino, California
City Attorney Carol Korade
20410 Town Center Lane #210
Cupertino, CA 95014-3220

City of Sunnyvale, California
City Attorney David Kahn
456 W. Olive Ave.
Sunnyvale, CA 94086

City of Mountain View, California
City Attorney Jannie Quinn
500 Castro Street
Mountain View, CA 94039-7540

EXHIBIT 16

DECLARATION OF SOEUN PARK KRATTER

I, Soeun Park Kratter, declare as follows:

1. I currently reside at 10536 Manzanita Court in Cupertino, California. I have lived at this address with my family since September 2010.

2. I am currently a member of No Toxic Air, Inc., a group of citizens of Santa Clara County concerned about the harmful effects of toxic substances emitted from Lehigh Southwest Cement Company's ("Lehigh") Permanente Facility, a limestone quarry and Portland cement manufacturing facility located at 24001 Stevens Creek Boulevard in Cupertino, California (the "Facility").

3. My residence is located approximately one mile from the Facility. Operation of the Facility significantly and negatively impacts my use and enjoyment of my property and home. The Facility's emissions of toxic substances also pose a grave concern to me concerning the associated health impacts on myself and my family.

4. The Facility's emissions leave a visible coating of dust on my car, patio furniture and the playground equipment used by my children. Knowing that this dust contains high levels of arsenic, lead, chromium VI and other dangerous substances, I am scared to let my children play in our back yard. Before I let my children touch anything left outdoors on our property, I feel compelled to wash it off with water and wipe it with a rag.

5. When the Facility's kiln is running, I can see a huge plume of smoke and dust headed over my neighborhood. Sometimes I can smell the fumes created when petroleum coke is burned to power the kiln. The odor reminds me of the way the freeway smells when there is a large traffic jam in the summer.

6. The most worrisome thing about the Facility is that it emits hundreds of pounds of mercury into the atmosphere, but I can't detect that with my senses, even though I know it is occurring. As a result, on many occasions I have decided not to take my nine-month-old baby

for a walk outside, particularly when I can see a plume of smoke and dust emanating from the plant.

Executed on February 3, 2011, in Cupertino, California.

SOEUN PARK KRATTER

EXHIBIT 17

DECLARATION OF ANISA RANGWALA

I, Anisa Rangwala, declare as follows:

1. I currently reside at 10788 Juniper Court in Cupertino, California. My family and I recently moved to this address in April 2010.

2. I am currently a member of No Toxic Air, Inc., a group of citizens of Santa Clara County concerned about the harmful effects of toxic substances emitted from Lehigh Southwest Cement Company's ("Lehigh") Permanente Facility, a limestone quarry and Portland cement manufacturing facility located at 24001 Stevens Creek Boulevard in Cupertino, California (the "Facility").

3. My residence is located approximately one mile from the Facility. Operation of the Facility significantly and negatively impacts my use and enjoyment of my property and home. The Facility's emissions of toxic substances also pose a grave concern to me concerning the associated health impacts on myself and my family.

4. My family and I are very concerned that the Facility is located in a densely populated area so close to our home. The Facility is polluting our air with mercury, a known neurotoxin. Additionally, I understand that the Facility has been operating without a valid Title V Permit since 1996.

5. At a Cupertino City Council meeting held on December 21, 2010, a Lehigh official mentioned that limestone mined at the Facility is very rich in mercury and that the Facility's mercury emissions are very difficult to control. If this is the case, the Facility's operations should not be allowed to continue. I find it extremely concerning that Lehigh is currently applying for a new open pit mine over 200 acres in size at the Facility.

6. Based on the Facility's air emissions, particularly mercury, we are very worried about the health of our children and Santa Clara County residents in general.

Executed on February 3rd, 2011, in Cupertino, California.

Anisa Rangwala

ANISA RANGWALA

EXHIBIT 18

DECLARATION OF JANET GEIGER

I, Janet Geiger, declare as follows:

1. I currently reside at 10240 Dubon Avenue in Cupertino, California. I have lived at this address with my family since 2001.

2. I am currently a member of No Toxic Air, Inc., a group of citizens of Santa Clara County concerned about the harmful effects of toxic substances emitted from Lehigh Southwest Cement Company's ("Lehigh") Permanente Facility, a limestone quarry and Portland cement manufacturing facility located at 24001 Stevens Creek Boulevard in Cupertino, California (the "Facility").

3. My residence is located approximately 1-2 miles from the Facility. Operation of the Facility significantly and negatively impacts my use and enjoyment of my property and home. The Facility's emissions of toxic substances also pose a grave concern to me concerning the associated health impacts on myself and my family.

4. My family and I suffer from dust created by the Facility in many ways. It settles everywhere and combines with the morning dew to form a patina of cement on everything outside, including our cars, patio furniture and trailers. Dust from the Facility also gets in our lungs. We can smell what appears to be gunpowder used in the blasting conducted at the Facility's quarry, which strongly suggests we are breathing in other harmful chemicals and particulate matter as well. My daughter needs a cortisone inhaler to relieve any upper respiratory ailments she gets in the winter, which I suspect are worsened by air emissions from the Facility.

5. I frequently observe plumes of smoke and dust rising high into the air above the Facility. Successfully reporting these occurrences is very difficult, because the inspectors from the Bay Area Air Quality Management District must have the sun at their back to legally measure the opacity of the plumes. Because the Facility is located on the west side of a valley, any plume inspected after Noon must be measured from the roads that wind into the hills behind the quarry. It takes a long time to drive to that area and in my experience, the inspectors have not able to successfully take such measurements as a result. Additionally, we cannot report any

emissions from the Facility that occur at night, despite the fact that the Facility's operations often continue for long periods after dark.

6. Lehigh does a significant amount of work at night and does so under very powerful flood lights. From my property and the surrounding neighborhood, I can plainly see the reflection from these bright lights if there is any cloud cover. As I am a bit of an amateur astronomer, I value a dark sky when viewing stars, a meteor shower or eclipse. This sort of activity is made virtually impossible when the Facility is operating after dark.

7. The Facility's operations also create a great deal of noise, which is most noticeable in the quiet of night. I prefer to sleep in quiet conditions. During the summer months, noise from the Facility can make sleeping with an open window difficult at my residence. Noise from the Facility's nighttime operations is also evident during the winter months when our windows are typically closed.

8. At times noise from the Facility is so loud that I have had to increase the volume on our television or radio to drown it out. The intensity of noise from the Facility varies depending upon wind direction and the particular operations being performed. There are many operations performed at the Facility that generate loud noises, ranging from bulldozer operation, blasting, running conveyor belts and crushing stone. These operations are louder than a freeway and include crashing, whirring and squealing sounds that sometimes persist all night long. The loud and sudden explosions from blasting done in the quarry are particularly unnerving.

9. There are numerous trucks coming and going from the Facility all day long. This truck traffic starts early in the morning. In addition to the sounds and smells common to large diesel-powered trucks, they stir up dust on the roadways and often have dust blowing out their uncovered beds. Disturbingly, many of these vehicles stop at the liquor store at the intersection of Foothill Boulevard and Stevens Creek Boulevard, and I have to wonder if the drivers are

///

///

///

buying alcohol and driving through our neighborhood while intoxicated.

Executed on February 3, 2011, in Cupertino, California.

JANET GEIGER

EXHIBIT 19

DECLARATION OF AVNER SCHWARZ

I, Avner Schwarz, declare as follows:

1. I currently reside at 21090 Canyon Oak Way in Cupertino, California. I have lived at this address with my family since December 2000.

2. I am currently a member of No Toxic Air, Inc., a group of citizens of Santa Clara County concerned about the harmful effects of toxic substances emitted from Lehigh Southwest Cement Company's ("Lehigh") Permanente Facility, a limestone quarry and Portland cement manufacturing facility located at 24001 Stevens Creek Boulevard in Cupertino, California (the "Facility").

3. My residence is located approximately one mile from the Facility. Operation of the Facility significantly and negatively impacts my use and enjoyment of my property and home. The Facility's emissions of toxic substances also pose a grave concern to me concerning the associated health impacts on myself and my family.

4. Dust accumulates very fast on furniture in our house – much faster than in any other home we have lived in previously. Consequently, we replace our air conditioning filters approximately every other month. While they are supposed to last for 3-4 months, they are visibly saturated with dust after only 2 months.

5. Our son is a sophomore at Monta Vista High School. He could ride his bicycle to school, but we do not allow him to do so because of the heavy truck traffic on Foothill Expressway, which is part of his route. This heavy truck traffic, which travels to and from the Facility, prevents us from safely using public streets in our neighborhood and causes us hardship.

Executed on February 3, 2011, in Cupertino, California.

AVNER SCHWARZ

EXHIBIT 20

DECLARATION OF RON YU

I, Ron Yu, declare as follows:

1. I currently reside at 21101 Canyon Oak Way in Cupertino, California. I have lived at this address with my family since 2000.

2. I am currently a member of No Toxic Air, Inc., a group of citizens of Santa Clara County concerned about the harmful effects of toxic substances emitted from Lehigh Southwest Cement Company's ("Lehigh") Permanente Facility, a limestone quarry and Portland cement manufacturing facility located at 24001 Stevens Creek Boulevard in Cupertino, California (the "Facility").

3. My residence is located approximately 1 mile from the Facility. Operation of the Facility significantly and negatively impacts my use and enjoyment of my property and home. The Facility's emissions of toxic substances also pose a grave concern to me concerning the associated health impacts on myself and my family.

4. The Facility's emissions leave a visible coating of dust on my patio furniture and other possessions stored outside. For example, I had to replace a pair of outdoor patio speakers after the toxic dust from the Facility turned them from their original white color to green. The retailer from whom I purchased the speakers said he had never seen anything like this color change before.

5. Additionally, the Facility's operations create disturbingly loud noises late at night, often from Midnight to 2 a.m.

Executed on February 3, 2011, in Cupertino, California.

RON YU

EXHIBIT 21

DECLARATION OF FLORICA ENESCU

I, Florica Enescu, declare as follows:

1. I currently reside at 23616 Oak Valley Road in the Oak Valley neighborhood of Cupertino, California. I have lived at this address with my family for the past eleven years.

2. I am currently a member of No Toxic Air, Inc., a group of citizens of Santa Clara County concerned about the harmful effects of toxic substances emitted from Lehigh Southwest Cement Company's ("Lehigh") Permanente Facility, a limestone quarry and Portland cement manufacturing facility located at 24001 Stevens Creek Boulevard in Cupertino, California (the "Facility").

3. My residence is located approximately 1-2 miles from the Facility. Operation of the Facility significantly and negatively impacts my use and enjoyment of my property and home. The Facility's emissions of toxic substances also pose a grave concern to me concerning the associated health impacts on myself and my family.

4. In the early years after we moved to our current residence, my family and I began to notice dust accumulating inside our home. We didn't think much of it at the time, and assumed it was due to the new construction being performed in the neighborhood and the dry hills surrounding the area.

5. However, over time we began to notice the gray dust accumulating inside our house, on furniture, picture frames, rugs, carpet, wood floors and window screens. We also observed dust accumulation outside on our outdoor patio furniture.

6. This dust is hard to notice at first because it is a very fine, light gray powder that easily disperses into the air just by breathing on it. We can see it floating in the air at certain times of the day when sunlight shines into our home.

7. We became quite concerned when we noticed this same gray dust on our furnace air filters and in the HEPA filter of our vacuum cleaner. In fact, I became so concerned that I started saving samples of dirt from my vacuum.

8. I am also extremely concerned how breathing this fine dust in our home might be impacting my health and my family's health, especially my young children.

9. Additionally, we have become very aware and uncomfortable with the sulfur-like odors often present in our neighborhood. Sometimes these odors are only slightly noticeable, while at other times they are quite noticeable and offensive.

10. Finally, we experience loud noises at our residence in the very early morning hours.

11. Due to the dust, odors and noise, we have to keep our windows closed.

12. It has become quite difficult to enjoy our beautiful home, the beautiful neighborhood in which we live, and Rancho San Antonio Park adjacent to us, when we have to worry about our health and the annoying and offensive elements around us.

Executed on February 3rd, 2011, in Cupertino, California.

Florica Enescu

FLORICA ENESCU

EXHIBIT 22

DECLARATION OF THORSTEN von STEIN

I, Thorsten von Stein, declare as follows:

1. I currently reside at 22608 Poppy Drive in Cupertino, California. I have lived at this address since 2008.

2. I am currently a member of No Toxic Air, Inc., a group of citizens of Santa Clara County concerned about the harmful effects of toxic substances emitted from Lehigh Southwest Cement Company's ("Lehigh") Permanente Facility, a limestone quarry and Portland cement manufacturing facility located at 24001 Stevens Creek Boulevard in Cupertino, California (the "Facility").

3. My residence is located approximately one mile from the Facility. The Facility's so-called East Material Storage Area is visible from parts of my property. Operation of the Facility significantly and negatively impacts my use and enjoyment of my property and home.

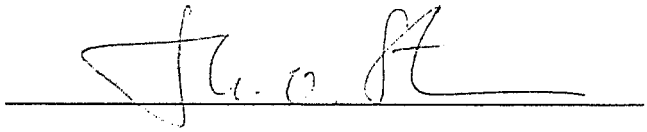
4. The neighborhood is generally very quiet, despite the relative proximity of the Interstate 280 freeway, which is only rarely audible. Traffic noise from Foothill Boulevard is greatly attenuated by a small ridge between that street and my house.

5. On some nights, typically during early morning hours and often on weekends, an intense fan-like sound is heard at my residence. This sound has the tendency to swell on and off periodically, and, when it is present, it lasts for many hours, usually abating in the late morning hours.

6. The fan-like sound mentioned above is sometimes accompanied by a penetrating, low-pitch grinding sound. This noise far exceeds in intensity any other ambient noise in the neighborhood. It requires closing windows in the summer, but often remains clearly audible even through closed windows. It has caused me several sleepless nights over the past three years.

7. While I cannot state with certainty that the Facility is the source of these disturbing sounds, I can provide no other logical explanation for them.

Executed on February 3rd, 2011, in Cupertino, California.



THORSTEN von STEIN, MD, PhD