Air Pollution and Health: A Quick Tour of the Scientific Evidence

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What are we breathing? Pure Air--nitrogen (78%),Oxygen (21%), Argon, CO₂... Various gaseous pollutants including: $-SO_2, NO_2, CO, O_3...$ Particulate matter: - Course particles (> 2.5 μ m in diameter) - Fine particles (< 2.5 μm in diameter) Other air toxics

How small are fine particles?





Magnified ambient particles (www.nasa.gov/vision/earth/environment)



Air pollution over SLC, UT



Donora, PA 1948

From, Public Health Service, Bulletin No. 306, 1949

- Th



Danora, PA. Noon, Oct 29, 1948.



London Fog Episode, Dec. 1952

THE BIG SMOKE



From: Brimblecombe P. The Big Smoke, Methuen 1987

Utah Valley

Winter inversions trap local pollution
Natural test chamber



Local Steel Mill, Utah Valley, 1989 ($PM_{10} = 150 \ \mu g/m^3$)

Utah Valley, 1989, ($PM_{10} = 50 \ \mu g/m^3$)

1111'89

Utah Valley, 1989, ($PM_{10} = 220 \ \mu g/m^3$)

Thermal bubble above smoke stack

ar 200 / Pars

There are real people down there, including children and elderly, breathing that stuff.

Children's Respiratory Hospital Admissions

Fall and Winter Months, Utah Valley



Sources: Pope. Am J Pub Health.1989; Pope. Arch Environ Health. 1991

Series of panel and related studies

Basic Questions asked: Are day-to-day changes in air pollution in Utah's Wasatch Front associated with changes in lung function, respiratory symptoms, medication use and/or school absences? Collaborators:

Dockery DW et al. (Harvard) Kanner RE (UofU) Ransom MR (BYU)

Sources:

Pope, et al. *Am Rev Resp Dis*.1991 Pope and Dockery. *Am Rev Resp Dis*.1992 Pope and Kanner. *Am Rev Resp Dis*. 1993 Ransom and Pope. *Environ Research*. 1992

Panel studies of asthmatics and non-asthmatics









Peak Flow and PM10 Pope et al, ARRD 1991

Panel study - 34 School Children -21 Asthma Patients Daily Peak Flow Measures (Evening) - Deviations from subject's mean Daily PM10 measurements - Max 195 ug/m3



Asthma Medication & PM10 Pope et al, ARRD 1991

Panel study - 34 School Children -21 Asthma Patients Daily Reports of Extra **Asthma Medications** Daily PM10 measurements - Max 195 ug/m3



Peak Flow and PM10 Pope & Dockery, ARRD 1992

Panel study

- 32 Symptomatic Children
 33 Asymptomatic Childrn
 Daily Peak Flow
 Measures (Evening)
 Deviations from subject's
 - mean
- Daily PM10 measurements
 - Max 251 ug/m3



Respiratory Symptoms and PM10

Pope & Dockery, ARRD 1992

Panel study 32 Symptomatic Children Daily Records of **Respiratory Symptoms** - Upper Respiratory Lower Respiratory - Cough Daily PM10 measurements - Max 251 ug/m3





Utah Valley Mortality Pope et al, Arch Env Hith, 1992

Daily deaths 1985-90 for Utah Valley Mean 2.7 per day Daily PM10 measures Mean 47 ug/m3 - Max 365 ug/m3 - Lo SO2, O3, NO2 Poisson Regression 1.5% per 10ug/m3



Summary of early Utah Valley epidemiological studies

Health effects

- Increased hospital admissions
- Increased respiratory symptoms
- Reduced lung function +
- Increased school absences,
- Increased respiratory and cardiovascular deaths



Study References

Pope (1989) Am. J. Public Health Pope (1991) Arch. Environ. Health

Pope, Dockery, Spengler, Raizenne (1991) Am. Rev. Resp. Dis. Pope, Dockery (1992) Am. Rev. Resp. Dis. Pope, Kanner (1993) Am. Rev. Resp. Dis.

Ransom, Pope (1992) Environ. Res

Pope, Schwartz, Ransom (1992) Arch. Environ. Health Pope, Kalkstein (1996) Environ. Health Perspect. Pope, Hill, Villegas (1999) Environ. Health Perspect.

An Association Between Air Pollution and Mortality in Six U.S. Cities

Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr, Speizer FE.

New England Journal of Medicine 1993

Methods:

14-16 yr prospective follow-up of 8,111 adults living in six U.S. cities.

> Monitoring of TSP PM_{10} , $PM_{2.5}$, SO_4 , H^+ , SO_2 , NO_2 , O_3 .

Data analyzed using survival analysis, including Cox Proportional Hazards Models.

Controlled for individual differences in: age, sex, smoking, BMI, education, occupational exposure.





Adjusted risk ratios (and 95% CIs) for cigarette smoking and $PM_{2.5}$

Cause of	Current Smoker,	Most vs. Least
Death	25 Pack years	Polluted City
All	2.00 (1.51-2.65)	1.26 (1.08-1.47)
Lung	8.00	1.37
Cancer	(2.97-21.6)	(0.81-2.31)
Cardio-	2.30	1.37
pulmonary	(1.56-3.41)	(1.11-1.68)
All	1.46	1.01
other	(0.89-2.39)	(0.79-1.30)

Particulate Air Pollution as a Predictor of Mortality in a Prospective Study of U.S. Adults

Pope CA III, Thun MJ, Namboodiri MM, Dockery DW, Evans JS, Speizer FE, Heath CW Jr.

Am J Respir Crit Care Med 1995



Methods: Linked and analyzed ambient air pollution data from 51-151 U.S. metro areas with risk factor data for over 500,000 adults enrolled in the ACS-CPSII cohort.



Adjusted mortality risk ratios (and 95% CIs) for cigarette smoking the range of sulfates and fine particles

Cause of Death	Current Smoker	Sulfates	Fine Particles
All	2.07 (1.75-2.43)	1.15 (1.09-1.22)	1.17 (1.09-1.26)
Lung	9.73 (5.96-15.9)	1.36	1.03
Cancer		(1.11-1.66)	(0.80-1.33)
Cardio-	2.28	1.26	1.31
Pulmonary	(1.79-2.91)	(1.16-1.37)	(1.17-1.46)
All other	1.54	1.01	1.07
	(1.19-1.99)	(0.92-1.11)	(0.92-1.24)



Showdown Over Clean Air Science Jocelyn Kaiser

Industry and environmental researchers are squaring off over studies linking air pollution and illness in what some are calling the biggest environmental fight of the decade



SPECIAL REPORT

H E A L T H E F F E C T S INSTITUTE

July 2000

Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality

A Special Report of the Institute's Particle Epidemiology Reanalysis Project

SUPREME COURT OF THE UNITED STATES

WHITMAN, ADMINISTRATOR OF ENVIRONMENTAL PROTECTION AGENCY, ET AL. v. AMERICAN TRUCK-ING ASSOCIATIONS, INC., ET AL.

No. 99-1257. Argued November 7, 2000-Decided February 27, 2001*

Legal uncertainty largely resolved with 2001 unanimous ruling by the U.S. Supreme Court.



Lung Cancer, Cardiopulmonary Mortality, and Long-term Exposure to Fine Particulate Air Pollution

JAMA, March 6, 2002-Vol 287, No. 9

C. Arden Pope III, PhD
Richard T. Burnett, PhD
Michael J. Thun, MD
Eugenia E. Calle, PhD
Daniel Krewski, PhD
Kazuhiko Ito, PhD
George D. Thurston, ScD





Context Associations have been found between day-to-day particulate ai and increased risk of various adverse health outcomes, including cardiopulmc tality. However, studies of health effects of long-term particulate air pollubeen less conclusive.

Objective To assess the relationship between long-term exposure to fir late air pollution and all-cause, lung cancer, and cardiopulmonary mortalit

Design, Setting, and Participants Vital status and cause of death data lected by the American Cancer Society as part of the Cancer Prevention II stu going prospective mortality study, which enrolled approximately 1.2 million adu







Figure 2. Nonparametric Smoothed Exposure Response Relationship





Figure 1. Level of Exposure to Fine Particulate Matter and the Risk of Death from Cardiovascular Causes in Women.

The graphs demonstrate the observed relationship between the risk of death from cardiovascular disease and the level of particulate matter of less than 2.5 µm in aerodynamic diameter (PM_{2.5}), including both definite and possible deaths from coronary heart disease or cerebrovascular disease. Panel A shows the overall relationship between the PM_{2.5} level and death, Panel B the effects between metropolitan areas, and Panel C the effects within metropolitan areas, with an indicator variable used to adjust for each city. These results

suggest a generally linear relationship between exposu extremes of exposure. Risk is depicted in comparison wi trates the density of exposure distribution for air pollut household income, smoking status, systolic blood pres tension, or hypercholesterolemia.

Miller et al. Long-Term exposure to Air Pollution and Incidence of Cardiovascular Events in Women. NEJM 2007

Air Pollution: Bad For Your Heart

DALLAS, Dec. 16, 2003



(AP) Air pollution in U.S. cities causes twice as many deaths from heart disease as it does from lung cancer and other respiratory ailments, a surprising new study suggests.



Can this really be true?—is it biologically plausible?

(AP / CBS)

OUOTE

"It certainly did st anticipated that b your lungs would direct impact on y C. Arden Pope III, B

If so, how?—what are the pathopysiological pathways that observed these real link breathing air pollution and cardiovascular deaths?

Effects of fine PM on the -



 Lungs
 Pulmonary Inflammation
 Reduced lung function
 Increased respiratory symptoms
 Accelerated progression and exacerbation of COPD



Southern California Children's Health Study

Effects of air pollution on children's health, especially lung function growth.





W. James Gauderman



John Peters



Gauderman et al. The effect of air pollution on lung development from 10 to 18 years of age. *New England Journal of Medicine* 2004



Figure: Percent-predicted lung function at age 18 years versus residential distance from a freeway. The horizontal line at 100% corresponds to the referent group, children living > 1500 m from a freeway.

Gauderman et al. Effect of exposure to traffic on lung development from 10 to 18 years of age: a cohort study. *Lancet* 2007

Effects of fine PM on -



Blood Markers of Systemic Inflammation and Oxidative Stress

Increased CRP
Proinflammatory mediators
Leukocyte & platelet activation
Increased blood coagulability

Effects of fine PM on

Cardiac Autonomic function and Cardiac Arrythmia





Effects of fine PM on

Blood Vessels (vasculature)

 Endothelial dysfunction
 Atherosclerosis
 (accelerated progression and destabilization of plaques)

Heart

Increased Ischemic Heart Disease (including MIs or heart attacks)

Brain

Increased Cerebrovascular ischemia (including ischemic strokes)

Pope and Dockery, JAWMA 2006.

Heart

- Altered cardiac autonomic function
 Increased dysrhythmic susceptibility
- Altered cardiac repolarization
 Increased myocardial ischemia

Vasculature 4

 Atherosclerosis,
 accelerated progression of and destabilization of plaques
 Endothelial dysfunction

Vasoconstriction and Hypertension

PM Inhalation

Lungs

- Inflammation
- Oxidative stress
- Accelerated progression
- and exacerbation of COPD
- Increased respiratory symptoms
 - Effected pulmonary reflexes
 - Reduced lung function

Blood

- Altered rheology
- Increased coagulability
- Translocated particles
- Peripheral thrombosis
- Reduced oxygen saturation

Systemic Inflammation Oxidative Stress

- Increased CRP
- Proinflammatory mediators
- Leukocyte & platelet activation

Brain

 Increased cerebrovascular ischemia



So what does this have to do with air pollution?

Fine Particulate exposure **Pulmonary and** systemic inflammation and oxidative stress (along with blood lipids) **Progression and** destabilization of atherosclerotic plaques



Plaque with fibrous cap





Blood clot forms around the rupture, blocking the artery





A series of studies (1997-2002) by Stephan van Eeden, James Hogg, and others found that in rabbits naturally prone to develop atherosclerosis,

Fine particulate exposure ↓↓ Accelerated progression of atherosclerotic plaques with greater vulnerability to plaque rupture



Stephan van Eeden



James Hogg

Sun et al. (JAMA 2005)

Representative Photomicrographs of Aortic Arch Sections



Example 1. Souza, Saldiva, Pope, Luiza. Chest 1998



Example 2. Pope, et al. *Circulation* 2004 Cardiovascular Mortality and Long-Term Exposure to Particulate Air Pollution

Epidemiological Evidence of General Pathophysiological Pathways of Disease



Example 3: Kunzli et al. EHP 2005



Example 4.

Ischemic Heart Disease Events Triggered by Short-Term Exposure to Fine Particulate Air Pollution

C. Arden Pope III, PhD; Joseph B. Muhlestein, MD; Heidi T. May, MSPH; Dale G. Renlund, MD; Jeffrey L. Anderson, MD; Benjamin D. Horne, PhD, MPH

Circulation. 2006;114-2443-2448.

Methods:

Case-crossover study of acute ischemic coronary events (heart attacks and unstable angina) in 12,865 well-defined and followed up cardiac patients who lived on Utah's Wasatch Front.



Jeffrey Anderson

Left coronary Right coronary arteru Left artery (CA) RCA) circumflex artery (LCX) Pamus. inter medius anterior cending art. Diagnonal branch, LAD Acute marginal branches, RCA Posterior descending artery (PDA)

Using cardiac angiography, cardiologists can obtain images of the arteries of the heart.

Left anterior descending __ coronary artery

Lesion blocking LAD

Left circumflex_ coronary artery

The NEW ENGLAND JOURNAL of MEDICINE



Air Pollution and Health — Good News and Bad

C. Arden Pope III, Ph.D.

NEJM 2004

From at least one perspective, these results are good news—

Air pollution is just one of many risk factors for cardiopulmonary disease, but it is a risk factor that can be modified and controlled.



Mortality Effects of a Copper Smelter Strike and Reduced Ambient Sulfate Particulate Matter Air Pollution

Pope et al. EHP 2007





Beijing commuters, Dec. 14, 2004. (Reuters/ReinhardKrause files, Science News, Jan. 25,2007)

