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:
  - SO₂, NO₂, CO, O₃...

- **Particulate matter**:
  - Course particles (> 2.5 μm in diameter)
  - **Fine particles** (< 2.5 μm in diameter)

- Other air toxics
How small are fine particles?

- Human Hair (60 μm diameter)
- PM$_{10}$ (10 μm)
- PM$_{2.5}$ (2.5 μm)
Magnified ambient particles (www.nasa.gov/vision/earth/environment)
Electron Microscope images of soot particles

From:
Park K, Cao F, Kittelson DB, McMurry PH.
Environ Sci Technol 2003
Air pollution over SLC, UT
Donora, PA 1948

From, Public Health Service,
Bulletin No. 306, 1949
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 μg/m$^3$)
Utah Valley, 1989, (PM$_{10}$ = 50 µg/m$^3$)
Utah Valley, 1989, ($PM_{10} = 220 \, \mu g/m^3$)

Thermal bubble above smoke stack
There are real people down there, including children and elderly, breathing that stuff.
Children's Respiratory Hospital Admissions
Fall and Winter Months, Utah Valley

PM$_{10}$ concentrations

- Mean PM$_{10}$ levels for Months Included
- Mean High PM$_{10}$ levels for Months Included

Children's respiratory hospital admissions
- Bronchitis and Asthma
- Pneumonia and Pleurisy
- Total

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?

Sources:

Collaborators:
Dockery DW et al. (Harvard)
Kanner RE (UofU)
Ransom MR (BYU)
Panel studies of asthmatics and non-asthmatics
Fig. 1. Daily PM$_{10}$ levels, mean peak expiratory flow deviations (ΔPEF), percentage who reported cough, and number of participants for the symptomatic sample.
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 μg/m³

![Graph showing the deviation in PEF (L/min) against PM10 levels with data points for Patients and School.]
Asthma Medication & PM$_{10}$

*Pope et al, ARRD 1991*

- Panel study
  - 34 School Children
  - 21 Asthma Patients
- Daily Reports of Extra Asthma Medications
- Daily PM$_{10}$ measurements
  - Max 195 ug/m$^3$

% Using Extra Medication

![Graph showing the relationship between PM$_{10}$ levels and the percentage of patients and school children using extra medication.](image)
Peak Flow and PM$_{10}$

Pope & Dockery, ARRD 1992

- Panel study
  - 32 Symptomatic Children
  - 33 Asymptomatic Children

- Daily Peak Flow Measures (Evening)
  - Deviations from subject's mean

- Daily PM$_{10}$ measurements
  - Max 251 ug/m$^3$
Respiratory Symptoms and PM$_{10}$

Pope & Dockery, ARRD 1992

- Panel study
  - 32 Symptomatic Children
- Daily Records of Respiratory Symptoms
  - Upper Respiratory
  - Lower Respiratory
  - Cough
- Daily PM$_{10}$ measurements
  - Max 251 ug/m$^3$
Utah Valley Mortality
Pope et al, Arch Env Hlth, 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**
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\textsubscript{10}, PM\textsubscript{2.5}, SO\textsubscript{4}, H\textsuperscript{+}, SO\textsubscript{2}, NO\textsubscript{2}, O\textsubscript{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$_{2.5}$

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Current Smoker, 25 Pack years</th>
<th>Most vs. Least Polluted City</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td><strong>2.00</strong> (1.51-2.65)</td>
<td><strong>1.26</strong> (1.08-1.47)</td>
</tr>
<tr>
<td>Lung Cancer</td>
<td><strong>8.00</strong> (2.97-21.6)</td>
<td><strong>1.37</strong> (0.81-2.31)</td>
</tr>
<tr>
<td>Cardio-pulmonary</td>
<td><strong>2.30</strong> (1.56-3.41)</td>
<td><strong>1.37</strong> (1.11-1.68)</td>
</tr>
<tr>
<td>All other</td>
<td><strong>1.46</strong> (0.89-2.39)</td>
<td><strong>1.01</strong> (0.79-1.30)</td>
</tr>
</tbody>
</table>
Particulate Air Pollution as a Predictor of Mortality in a Prospective Study of U.S. Adults


*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

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Current Smoker</th>
<th>Sulfates</th>
<th>Fine Particles</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>2.07 (1.75-2.43)</td>
<td>1.15 (1.09-1.22)</td>
<td>1.17 (1.09-1.26)</td>
</tr>
<tr>
<td>Lung Cancer</td>
<td>9.73 (5.96-15.9)</td>
<td>1.36 (1.11-1.66)</td>
<td>1.03 (0.80-1.33)</td>
</tr>
<tr>
<td>Cardio-Pulmonary</td>
<td>2.28 (1.79-2.91)</td>
<td>1.26 (1.16-1.37)</td>
<td>1.31 (1.17-1.46)</td>
</tr>
<tr>
<td>All other</td>
<td>1.54 (1.19-1.99)</td>
<td>1.01 (0.92-1.11)</td>
<td>1.07 (0.92-1.24)</td>
</tr>
</tbody>
</table>
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.
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
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 air and increased risk of various adverse health outcomes, including cardiopulmonary mortality. However, studies of health effects of long-term particulate air pollution been less conclusive.

**Objective**  To assess the relationship between long-term exposure to fine particulate air pollution and all-cause, lung cancer, and cardiopulmonary mortality.

**Design, Setting, and Participants**  Vital status and cause of death data collected by the American Cancer Society as part of the Cancer Prevention II study, a ongoing prospective mortality study, which enrolled approximately 1.2 million adults...
Figure 2. Nonparametric Smoothed Exposure Response Relationship

A All-Cause Mortality

B Cardiopulmonary Mortality

C Lung Cancer Mortality

D All Other Cause Mortality
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 exposure extremes of exposure. Risk is depicted in comparison with the density of exposure distribution for air pollutants, household income, smoking status, systolic blood pressure, or hypercholesterolemia.
Can this really be true?—is it biologically plausible?
If so, how?—what are the pathophysiological pathways that 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

David Bates, Advisor
Gauderman et al. The effect of air pollution on lung development from 10 to 18 years of age. *New England Journal of Medicine* 2004
Blood Markers of Systemic Inflammation and Oxidative Stress

• Increased CRP
• Proinflammatory mediators
• Leukocyte & platelet activation
• Increased blood coagulability

Effects of fine PM on
Effects of fine PM on Cardiac Autonomic function and Cardiac Arrhythmia
Effects of fine PM on

Heart
- Increased Ischemic Heart Disease (including MIs or heart attacks)

Blood Vessels (vasculature)
- Endothelial dysfunction
- Atherosclerosis (accelerated progression and destabilization of plaques)

Brain
- Increased Cerebrovascular ischemia (including ischemic strokes)
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

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

Vasculature
- Atherosclerosis, accelerated progression of and destabilization of plaques
- Endothelial dysfunction
- Vasoconstriction and Hypertension

Systemic Inflammation
Oxidative Stress
- Increased CRP
- Proinflammatory mediators
- Leukocyte & platelet activation

Brain
- Increased cerebrovascular ischemia

Pope and Dockery, JAWMA 2006.
Clot Preventing Blood Flow

Plaque Buildup

Site Of Blockage In Coronary Artery

Affected Area Of The Heart
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
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**
Sun et al. (JAMA 2005)

Representative Photomicrographs of Aortic Arch Sections

<table>
<thead>
<tr>
<th>Normal Chow</th>
<th>High-Fat Chow</th>
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<tr>
<td>Clean Filtered Air</td>
<td>Clean Filtered Air</td>
</tr>
<tr>
<td>PM Polluted Air</td>
<td>PM Polluted Air</td>
</tr>
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</table>

The images show representative photomicrographs of aortic arch sections from rats fed normal and high-fat chow, exposed to clean filtered air or PM polluted air.

**Cardiovascular Mortality and Long-Term Exposure to Particulate Air Pollution**

**Epidemiological Evidence of General Pathophysiological Pathways of Disease**

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John Godleski
Example 3: Kunzli et al. *EHP* 2005

Ursula Ackermann-Liebrich and Nino Kunzli
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.
Using cardiac angiography, cardiologists can obtain images of the arteries of the heart.
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.
Six Cities Cohort Follow-up

Mortality Risk Ratio vs. PM$_{2.5}$ (μg/m$^3$)

Steubenville, Topeka, Kingston, Portage, Watertown, St. Louis

Laden et al, AJRCCM 2006
Mortality Effects of a Copper Smelter Strike and Reduced Ambient Sulfate Particulate Matter Air Pollution

Pope et al. EHP 2007