Which PM Components Affect Cardiovascular Health and How Do They Vary by Region?

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Ambient Particles Come From Many Sources
What is Particulate Matter?

• Products of combustion, atmospheric reactions, and mechanical processes

• Health Research Concerns for PM
  – Wide range of particle sizes
  – Wide range of physicochemical properties
  – Wide range of health impacts, including cardiopulmonary morbidity and mortality
Overview

• Epidemiology and toxicology studies linking PM to cardiovascular disease (CVD)
  – Evidence for role of PM components in CVD

• NYU research

• Current research area
  – Role of particle size, season, region, and components in PM toxicity
PM and CVD

• Specific association of PM with:
  – ischemic heart disease
  – congestive heart failure
  – arrhythmias

• Heart failure deaths make up 10% of all cardiovascular deaths, but account for 30% of cardiovascular deaths related to PM exposure

• Of the 350,000 sudden cardiac deaths in the US per year, 60,000 are related to particulate air pollution
Mortality and Hospital Admissions are the “Tip of the Iceberg” of Pollution's Effects

- Premature Deaths (6,500)
- Hospitalizations (9,000)
- Respiratory Illness including Asthma (170,000)
- School Absence (1,300,000)
- Lost Workday (2,800,000)
Epidemiology studies linking PM to CVD

- Evidence for acute and chronic effects

- Evidence for role of PM components in CVD
Acute Effects – Time Series Epidemiology

• Throughout the U.S. and Europe
• California
Risk Estimates
(per increment of 10 µg/m³ in PM2.5 or PM10)
Are There Specific Components of PM Associated with Its Adverse Effects?
- Different chemical components vary by PM size
- PM size varies by different sources
Are There Regional Differences in PM's Effects?

• If so, it would imply a role for:
  – Source
  – Components
PM$_{2.5}$ and Medicare Hospital Admissions

Dominici, *JAMA* 2006
Excess Risk of Cardiovascular Mortality in CA
(interquartile range increase in PM2.5 mass and selected PM2.5 components)

Ostro B D, 2008
Excess Risk of Cardiovascular Mortality in CA
(interquartile range increase in PM2.5 mass and selected PM2.5 components)
Percent increase in health effects estimates for PM2.5 lag 0 and risk of cardiovascular hospitalizations per IQR increase in the fraction of PM2.5 total mass for each component

Bell M, 2009
Chronic Effects - Epidemiology
Figure 2. Mean CIMT ± 1 SE among quartiles of the PM$_{2.5}$ distribution. The y-axis shows mean CIMT levels at the population average of the adjustment covariates (age, sex, education, and income). The first quartile is the reference group.
Cardiovascular Mortality and Lung Cancer Affected by Long-Term Fine Particulate Matter

Relative Risks and 95%ile CI's for a 10 µg/m³ increase in annual PM$_{2.5}$ mass concentration. Size of the dot corresponds to the relative number of deaths.

Pope, JAMA, 2002
Range of Cardiovascular effects of PM

- Disruption of autonomic nervous system activity by decreased heart rate variability
- Arterial vasoconstriction
- Cardiac arrhythmias in patients with implantable defibrillators
- Cardiac events such as myocardial infarction
  - Elevated concentration of PM$_{2.5}$ transiently elevate the risk of MI within a few hours and 1 day after exposure
- Exacerbation of ST-segment changes in animal models of myocardial infarction
- Increased generation of CRP, white cell counts, fibrinogen, and plasma viscosity
- Increased CIMT
Potential Pathways for PM’s Effect on Cardiovascular System
Bottom Line

• How can PM cause adverse cardiovascular effects even in the absence of pulmonary effects?

Sub-clinical pulmonary effects

or

Soluble factors (or ultrafine PM) are transported to the cardiovascular system
NYU Research Collaborations

- Does long term exposure to PM$_{2.5}$ cause cumulative damage to cardiovascular, pulmonary, and other tissues?

- What is the relationship between the temporal variations in PM concentration or composition and acute changes in cardiac function?
Ambient Particle Concentrating and Animal Exposure System

- Ambient Air
- VACES (Sioutas, et al) Humidifier, Cooler, and Virtual Impactors
- Diffusion Dryer
- Animal Exposure Chambers (ECG telemetry monitoring)
Effect of Subchronic Exposures to Concentrated PM on Heart Rate in Mice

![Graph showing heart rate changes over time with dates from April to September, with data points and a trend line indicating a decrease in heart rate.](image)
Unusual changes in HR and HRV were associated with Ni, Cr, and Fe in Concentrated PM
PM that caused changes in HR and HRV was coming from the Northwest
Super Stack
Sudbury, Ontario Canada
Does the effect of nickel and vanadium hold up in an epidemiology study?
Nickel and Vanadium were only PM$_{2.5}$ components significantly associated with daily PM$_{10}$ mortality coefficients for 60 U.S. Cities.

Lippmann, 2006
CAPs exposure enhanced atherogenesis in mice fed a high fat chow, with accompanied increases in lipid content (ORO staining)
Summary

PM is associated with significant increases in adverse cardiovascular effects

But how important are these changes?
Why is a PM-driven small per cent increase in cardiovascular morbidity and mortality so important?

Deaths and hospital discharges from diseases of the heart (U.S.: 1900–2005).
Current Research - Gordon Lab
Percent of PM$_{2.5}$ composition by component for yearly, winter, and summer averages, by region
Percent of PM$_{2.5}$ composition by component for yearly, winter, and summer averages, by region.
The Multi-City Ambient PM Study (MAPS)

Seattle
Utah
Sterling Forest
Hunter College
South Bronx
Phoenix
Effect of PM on Reactive Oxygen Species Production in Airway Epithelial Cells

Dose = 50 µg/ml

HC: Hunter College
SF: Sterling Forest
SB: South Bronx
PH: Phoenix
UT: Utah
SE: Seattle
Effect of Aspirated PM in Mice

PMNs

S = Seattle
U = Utah
B = Bronx
SF = Sterling Forest

Gilmour, 2007
Comparative toxicity of coarse particles

PI: Terry Gordon

Co-I: Kaz Ito, Mort Lippmann, Lung Chi Chen
Objective

• To determine the contribution of coarse particles to the adverse effects associated with exposure to ambient PM

• We hypothesize that differences in the toxicity of coarse PM (PM$_{10-2.5}$) samples are due to the source contributions of the particles
Experimental Design

- Design was copied from European scientists (Netherlands/Germany)
- Measure the differential toxicity of coarse particles both *in vitro* and *in vivo*
- Identify whether coarse particles from urban and rural sources differ in toxicity.
Collection Apparatus

[Image of a diagram showing the collection apparatus with labeled stages: Rain Cap, PM-10 Stage (Greased or PUF), PM-2.5 PUF Stage, PM-0.1 PUF Stage, Ultrafine Filter Stage, and an Exit arrow.]
Study Design (cont....)

• Several sites in urban and rural NY and Central California
• Winter and summer
• 2 particle sizes (coarse and fine/UF)
  – Co-located teflon and quartz filter samples
• *In vivo* bioassay - mouse
• *In vitro* bioassay - 3 cell types
  – epithelial, vascular endothelial, cardiac myocytes
Rural Enough?
Effects by Size and Season

Normalized ROS production

Ultra Coarse
Coarse
Fine

Summer
Winter
Effect of Size and City

Normalized ROS production

- Ultracoarse
- Coarse
- Fine

Cities:
- Bronx
- Goshen
- Manhattan
- Tuxedo
- Wallkill

Values:
- ND
- ND
- ND
Conclusions (NY only)

- Size, season, and site (urban vs. rural) were shown to be significant factors influencing ROS production *in vitro*.
- Generally, the coarse fraction elicited a greater ROS response than either fine or 'super coarse' PM.
- Generally, coarse PM collected in Winter elicited a greater ROS response than that collected in Summer.
- Generally, urban coarse samples (i.e., Bronx and Manhattan) produced greater effects than rural samples.
- Analysis of PM composition needs to be considered to gain a better understanding of these effects.
CALIFORNIA AIR SAMPLING
PM COLLECTED (mean per stage over 48 hrs)
CALIFORNIA AIR SAMPLING
MAX PM COLLECTED (per stage over 48 hrs)
Work To Be Completed in the Next Year

• *In vitro* and *in vivo* bioassays on California samples
• Chemical analyses on NY and California samples
• Source apportionment
• Correlation of components and sources with *in vitro* and *in vivo* effects
Health Effects Institute

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