Vascular consequences of inhaled particulate matter: Vulnerability in health and disease

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AN ASSOCIATION BETWEEN AIR POLLUTION AND MORTALITY IN SIX U.S. CITIES

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When mortality from all causes was considered, or when deaths due to cardiovascular and respiratory diseases were grouped together, the effects of air pollution were consistent and the association was robust.
Six Cities Study and Beyond

“Air pollution kills.”

Since then, a steady stream of studies has grown into a river of reports that collectively have swelled the banks of this initial association and have further specified that ischemic heart disease is the single-most abundant cause of morbidity related to air pollution.

Conklin D J Circulation Research 2011;108:644-647
Mechanism of PM2.5 induction of vascular inflammation/dysfunction.

Conklin D J Circulation Research 2011;108:644-647
JUST SAY NO

MOLECULE OF THE YEAR
\[
\overset{\text{N=O}}{\text{NO}}
\]
Endothelium mediated vasodilation and NO bioavailability

L-Arginine → eNOS → Citrulline

Endothelium

NO → ONOO⁻

O₂⁻

NO

sGCi → sGCa → cGMP → GTP → RELAXATION

Smooth muscle cell
Flow-mediated dilation (FMD)

- Ischemia
- Hyperemia
- Vasodilation
Passive limb movement (PLM)
PM Pollution and Cardiovascular Function in Health and COPD

\[ \text{PM}_2.5 \rightarrow \text{Inflammation} \uparrow, \text{Free Radicals} \uparrow, \text{Oxidative Stress} \uparrow \rightarrow \text{Nitric Oxide} \downarrow \rightarrow \text{CV Function} \downarrow \]
PM$_{2.5}$ in Salt Lake City during Winter 2013-2014

Polluted Air Experiments

Clean Air Experiments
Methods

Experimental Protocol: Controls: N=3  COPD: N=5

Pulmonary Function

Blood Draw

Vascular Function Assessments

Flow Mediated Dilation (FMD)

Passive Limb Movement (PLM)

Inflammatory Markers

Oxidative Stress Markers

NO Bioavailability

FVC

FEV₁

FEV₁/FVC
Preliminary Results:
Pulmonary Function

FEV$_1$ (% Predicted)

- Control
- COPD

Clean Air
Polluted #1
Polluted #2
Preliminary Results:
Vascular Function: Flow Mediated Dilation

FMD (% Dilation)

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<th>Clean Air</th>
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Preliminary Results:
Vascular Function: Passive Limb Movement

Controls

COPD

Leg Blood Flow (ml/min) vs. Time (s)
Preliminary Results:
Summary

PM$_{2.5}$

…………but most clear effects in the healthy!
Future Directions

1. Continue the study this winter
2. Preventative Treatments?
Conundrum: Physical activity – Air Quality – CVD

“What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?”