

US EPA ARCHIVE DOCUMENT

# AMBIENT AIR POLLUTION EXPOSURE AND VASCULAR DYSFUNCTION

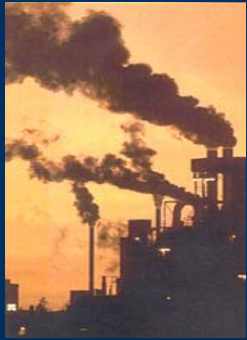


Robert D. Brook, MD  
Assistant Professor of Internal Medicine  
Division of Cardiovascular Medicine  
University of Michigan

# Cardiovascular Effects of PM

- **CAP exposures causes:**
  - Acute arterial vasoconstriction (Brook RD. Circulation 2002; 105:1534)
  - Increase in systolic blood pressure (Urch B. EHP 2005; 113: 1052)
  - Increase in ADMA (rats) (Dvonch JT. Inhalat Toxicol 2004; 16: 473)
  - Responses related to carbon (Urch B. Inhalat Toxicol 2004; 16: 345)
- **Ambient PM exposure causes:**
  - Increase in blood pressure (Zanobetti A. Circulation 2004; 110: 2184)
  - Impaired vascular function (O'Neill MS. Circulation 2005; 111: 2913)

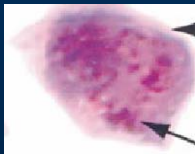
**PM<sub>2.5</sub>**



Organic, elemental carbon  
NH<sub>4</sub>SO<sub>4</sub> NH<sub>4</sub>NO<sub>3</sub>  
Fe Ni Cu Zn Cr V  
Biologic organisms



**Alveoli**



**ROS generation / oxidative stress**

Macrophage / alveolar cell PM uptake and activation  
PM induced (transition metals, organic agents)

**NF-κB activation**

Chemokine production (MCP-1, IL8, MIP-1α)  
Adhesion molecule expression (VCAM)  
Cytokine production (IL-6, TNFα)  
ROS generation (O<sub>2</sub><sup>-</sup>, H<sub>2</sub>O<sub>2</sub>, ONOO<sup>-</sup>)

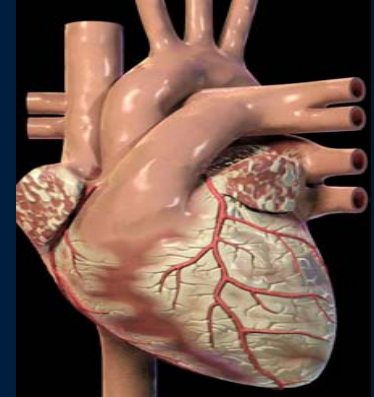
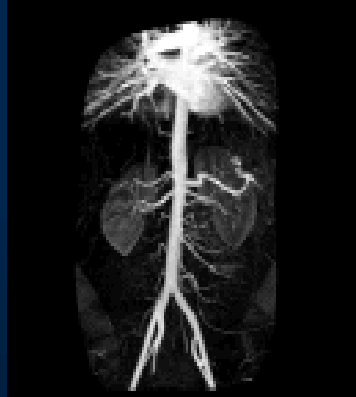
**Chronic**

**Acute**

- ↑ Activated WBC, Cytokines (IL-6, TNF, IL1β)
- ↑ Liver expression of CRP
- ↑ ROS vascular tissue/cellular generation
- ↑ Fibrinogen, platelet reactivity
- ? UFP in vessels, TF, Oxidized lipoproteins, insulin resistance

**Systemic oxidative stress  
Pro-inflammatory response**

- UFP in circulation
- Autonomic imbalance (direct PSNS/SNS reflex)
- ↑ ROS (PM, WBC, NADPH)
- ↑ Microparticles (Plt, cells)
- ↑ SNS, AT2-mediated ROS



**Vascular Dysfunction**

- Endothelial cell dysfunction (↓ NO<sup>•</sup>, eNOS)
- Vasoconstrictor expression (ET, ROS)
- Acute autonomic imbalance (↑ SNS)
- CAMs, Cytokines, oxLDL, mitogenic, WBC + Plt activation

**Atherosclerosis**

**Vasoconstriction**

# Ambient Air Pollution and Vascular Function

## DEARS Companion Study

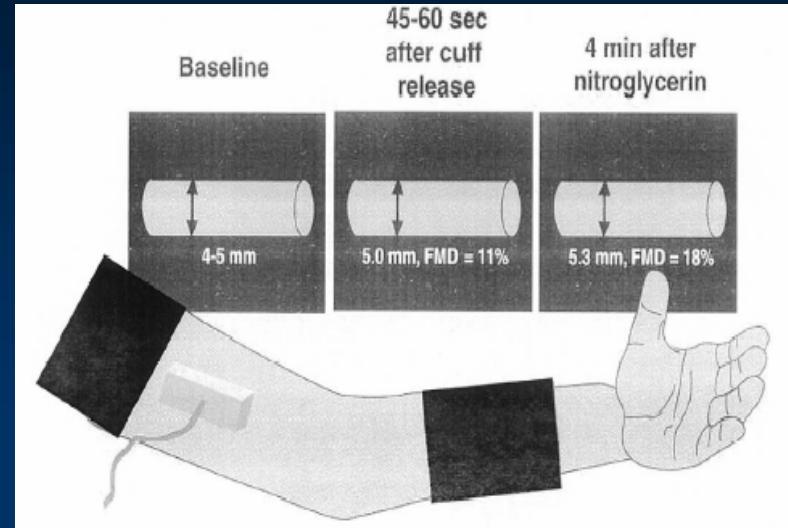
Do ambient levels of air pollutants effect vascular function in the real world?

- Relation of air pollutants to vascular function/BP
- Personal exposure monitoring (PM, OC, O<sub>3</sub>, metals)
- Determinants of response (BP, lipids, glucose)

## ***Vascular Companion Study to DEARS***

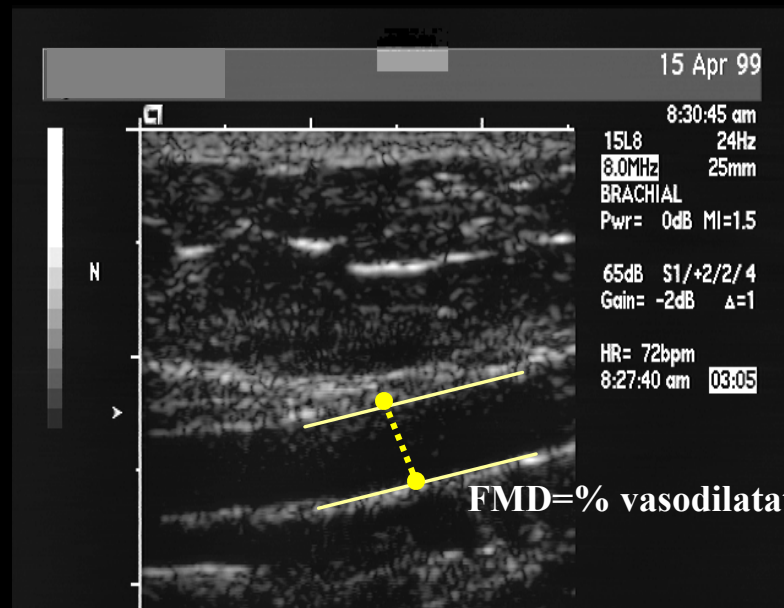
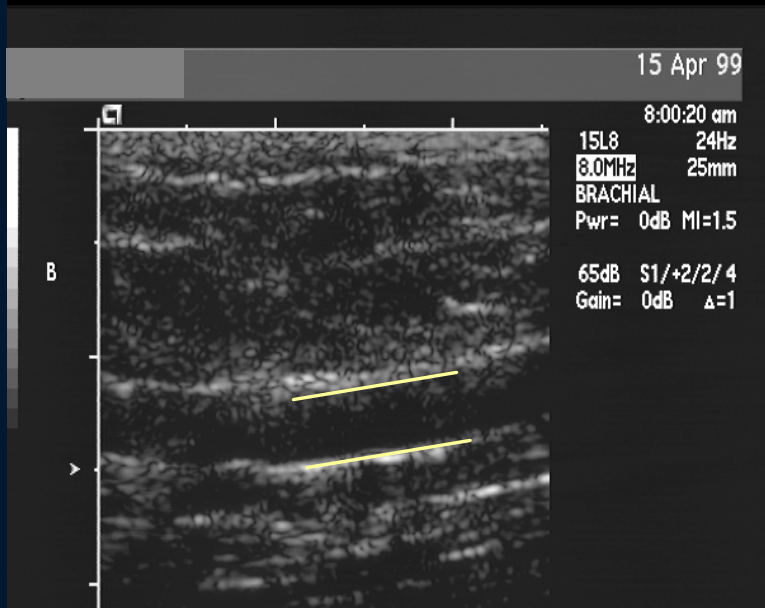
<b>Time of day</b>	<b>Activity</b>	<b>Duration</b>
6-9 am	Personal monitor device vests are given to the participant (Performed by DEARS monitors at the individual residence) Repeat on 2 <sup>nd</sup> participant at their residence Repeat on 3 <sup>rd</sup> participant at their residence	45 mins 45 mins 45 mins (3 hrs with travel time)
Between 6 and 9 am until 11 am	Subjects to wear personal monitor vests (Duration depends on order of receiving vest)	2-5 hrs
11am – 1 to 3 pm	Low-fat lunch (continue personal monitoring)	30-60 mins
1-3 pm until time between 6 and 9 pm	Subjects to wear personal monitor vests No additional food (fasting time period= 5 hours) (Duration may depend on order of vascular testing)	6-9 hrs
6-9 pm	Perform vascular testing in same order as receiving vests Perform vascular testing on 2 <sup>nd</sup> pt at their residence Perform vascular testing on 3 <sup>rd</sup> pt at their residence <b>**DAY ONE -- Measure cholesterol profile and blood glucose</b>	30 mins 30 mins 30 mins (3 hrs with travel time)

# Brachial Flow-Mediated Dilatation (FMD)



## BASELINE

## REACTIVE HYPEREMIA









# Study Status Through Season 3

Subjects consented	23 (49 potential) (47%)
Subjects completed	22
Winter 2005 / Summer 2005	9 / 13
Race and Ethnicity	5 Caucasian 4 Mexican American 13 African American
Gender	2 Male, 20 Female
Zip Code	48209--8
	48205--5
	48216--3
	48111--2
	48235--2
	48233--2

# Study Status Through Season 3

	Mean $\pm$ sd	Range
Age (years)	49 $\pm$ 18	21-80
Body Weight (kg)	87 $\pm$ 24	48-136
Body Mass Index (kg·m <sup>-2</sup> )	30.8 $\pm$ 8.10	16.8-47
Systolic BP (mm Hg)	135 $\pm$ 20	99-178
Diastolic BP (mm Hg)	79 $\pm$ 10	57-105
Heart rate (beats·min <sup>-1</sup> )	73 $\pm$ 12	48-103
<b>Medical History</b>	n (%)	
Coronary Artery Disease	1 (5%)	
Systemic Arterial Hypertension	11 (52%)	
Peripheral Artery Disease	2 (10%)	
Hyperlipidemia	8 (38%)	
Diabetes Mellitus	4 (19%)	
Positive CHD Family History	6 (29%)	

# Conclusions / Plans

- Measurement of vascular function/BP in the real world (home) environment is feasible and without adverse risk.
- Maintain High Retention:
  - 10/22 meeting
  - Commitment from most subjects (during follow-up)
  - Plan: Mail letter and follow-up call
- Improve initial enrollment for seasons 5-6