

# ASSESSMENT OF HEALTH HAZARDS OF REPEATED INHALATION OF DIESEL EMISSIONS, WITH COMPARISONS TO OTHER SOURCE EMISSIONS



**Joe Mauderly**  
(et many al.)

***NATIONAL ENVIRONMENTAL RESPIRATORY CENTER***

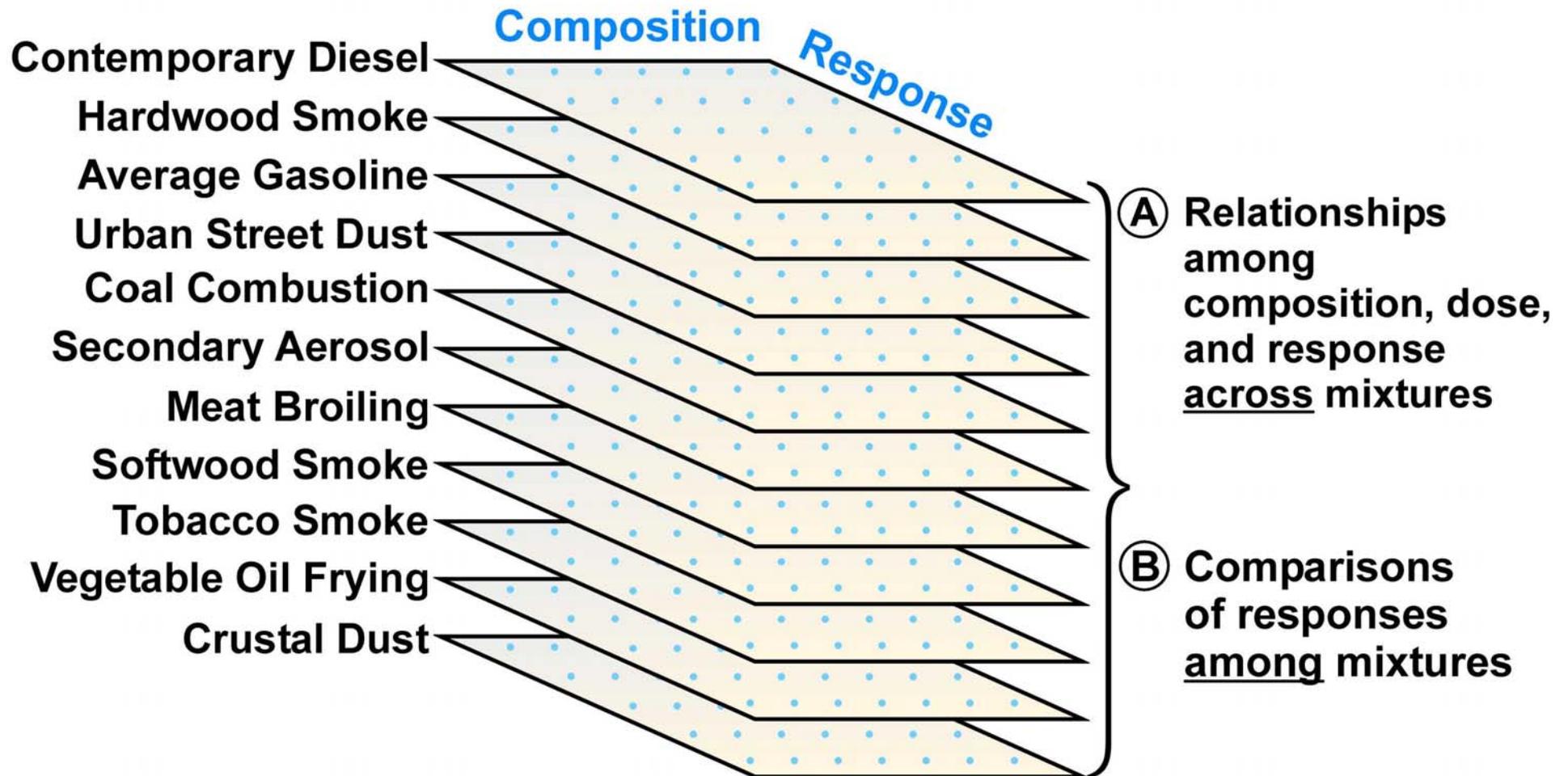
***Because you never breathe only one pollutant***

**Lovelace Respiratory Research Institute, Albuquerque, NM**



# NATIONAL ENVIRONMENTAL RESPIRATORY CENTER

Strategy: Build and analyze a composition-concentration-response data matrix



5082-1b



# STATUS OF THE NERC PROGRAM

Exposure to **diesel emissions** is completed, nearly all results analyzed, and several papers published

Exposure to **hardwood smoke** is completed, many data analyzed, and papers are in process

Exposure to **gasoline emissions** being initiated at this time

Exposure to **urban street dust** scheduled next. We are collecting dust

Exposure to simulated “downwind” **coal emissions** is planned, and key components of the atmosphere are defined

Exposure to simulated **secondary aerosol** (e.g., organic, sulfate, nitrate) is under discussion



# DIESEL EMISSIONS

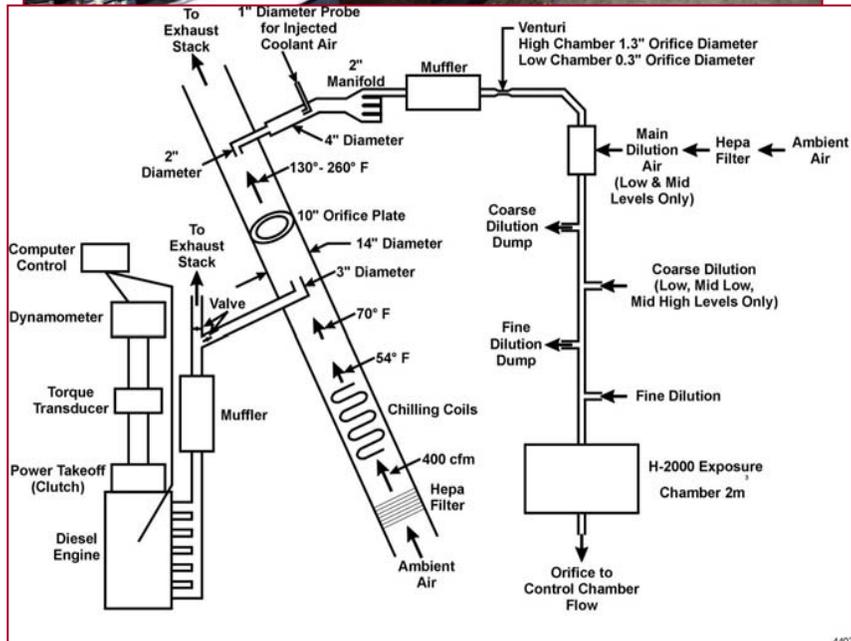


- 2000 Cummins 5.9L ISB 6 cyl. Turbo
- D-2 Cert. Fuel (370 ppm S, 29% aromatics)
- Shell Rotella® 15W-40 crankcase oil
- Stock exhaust system with muffler
- Repeated heavy-duty certification cycle
- Cold start excluded

Emissions diluted with carbon- and HEPA-filtered air

Expose at 1000, 300, 100, 30, 0  $\mu\text{g PM}/\text{m}^3$   
(dilutions  $\approx$  1:10 to 1:300)

(Now a baseline for “Clean Diesel”)



[Reed et al., *Inhal. Toxicol.* 16:177, 2004]  
[McDonald et al., *Env. Sci. Technol.* 38: 2513, 2004]



# HARDWOOD (OAK) SMOKE



Uncertified heating stove (Pineridge, 2 ft<sup>2</sup>)

Scaled room, air conditioned to absorb heat load

Oak from Missouri at 20% moisture

15 ft (4.6 m) stack from floor of stove

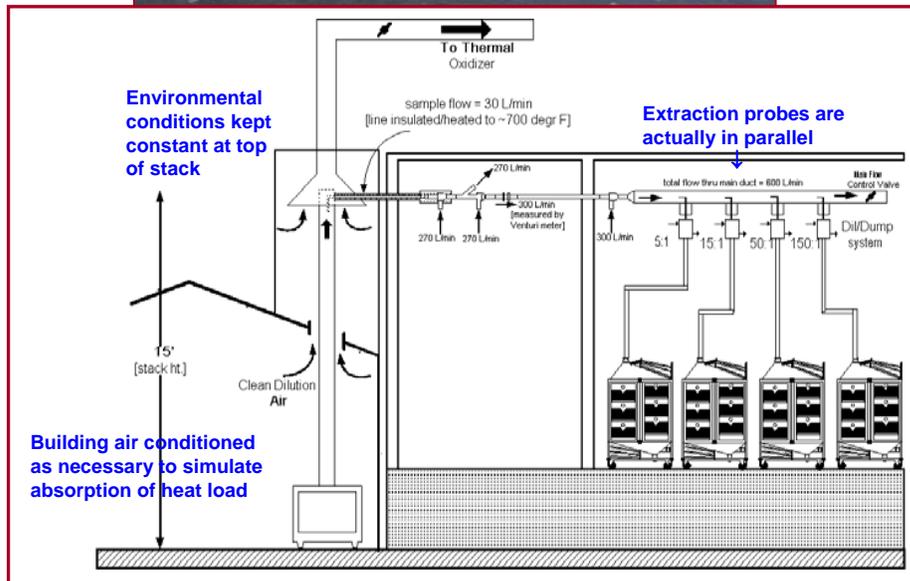
Constant draft conditions at top of stack

3-phase burn cycle

Extracted smoke 0.3 m from top of stack

Exposed at same PM mass concentration as diesel - 1000, 300, 100, 30, 0 µg/m<sup>3</sup>

(Dilutions ≈ 1:300 to 1:9000)

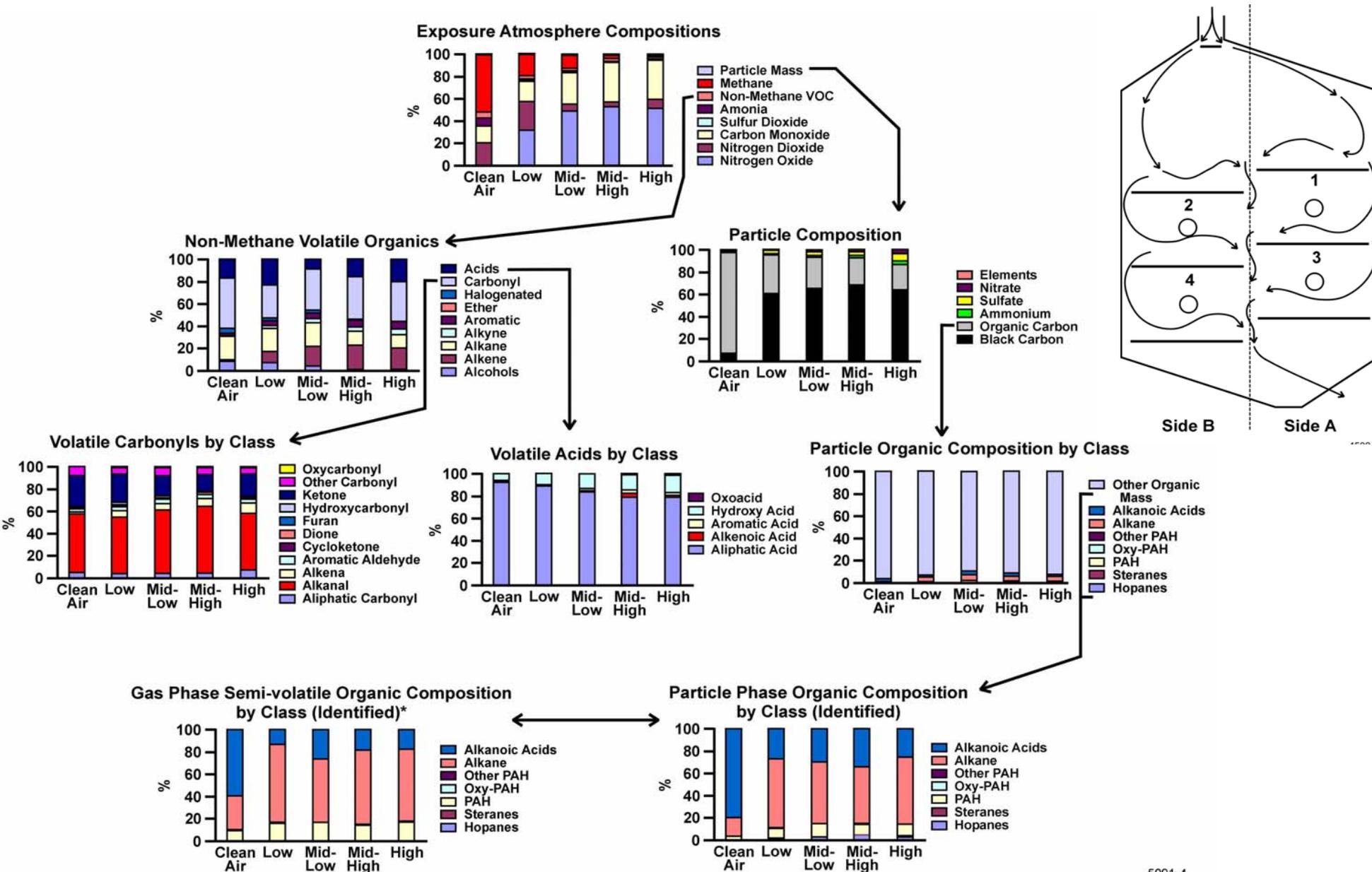


[Reed et al., *Am. J. Respir. Crit. Care Med.* 169:561, 2004]



# EXPOSURES ARE CHARACTERIZED IN DETAIL

(in the animal exposure chambers)



\*Semi-Volatile Organics not included in Mass Balance Above

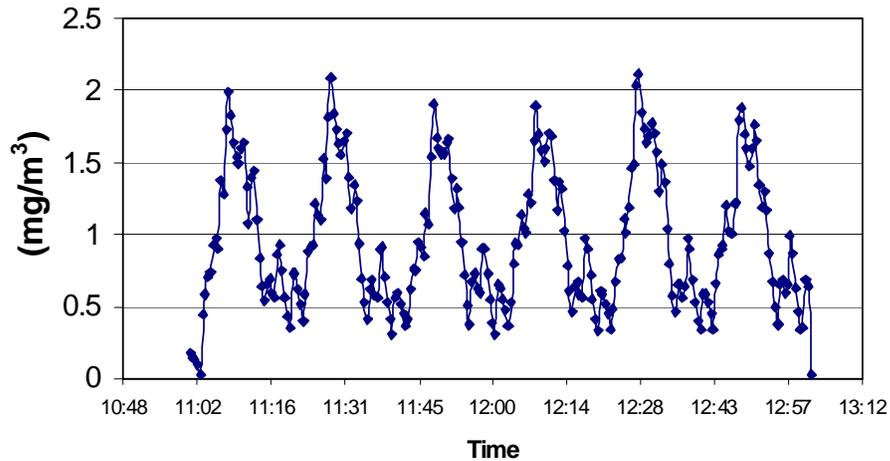
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# PARTICLE MASS AND NUMBER

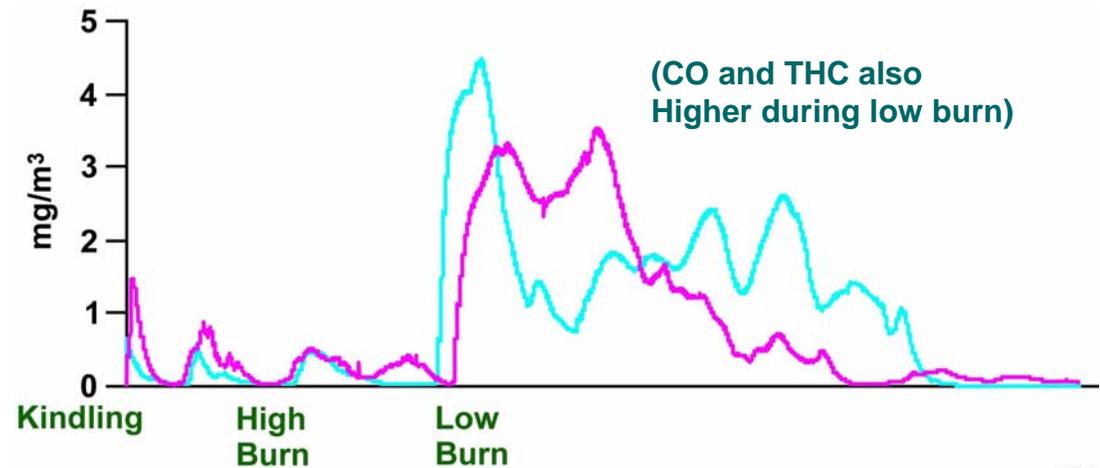
## Diesel

PM Concentration in High Level Chamber During Multiple Cycles



## Hardwood Smoke

PM Concentration in High Level Chamber During a 6-hr Day



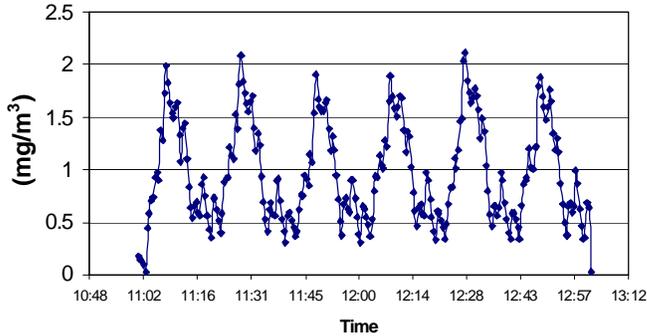
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# PARTICLE MASS AND NUMBER

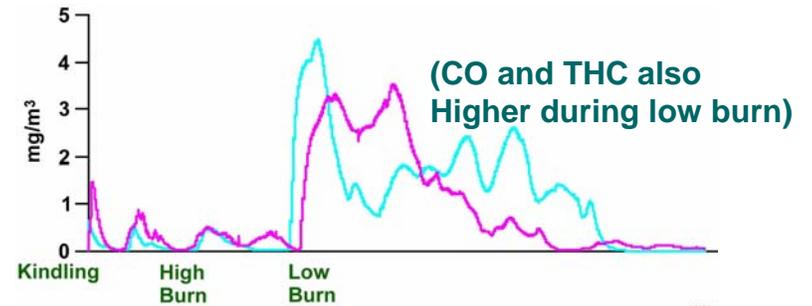
## Diesel

PM Concentration in High Level Chamber During Multiple Cycles



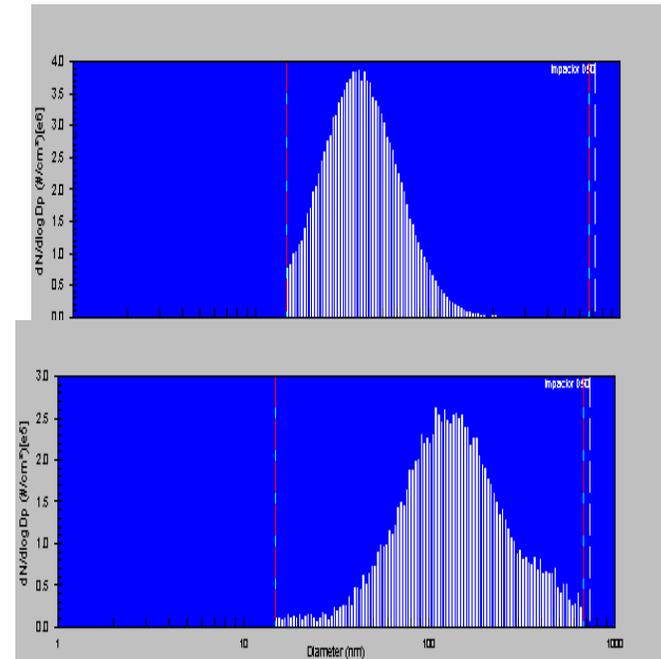
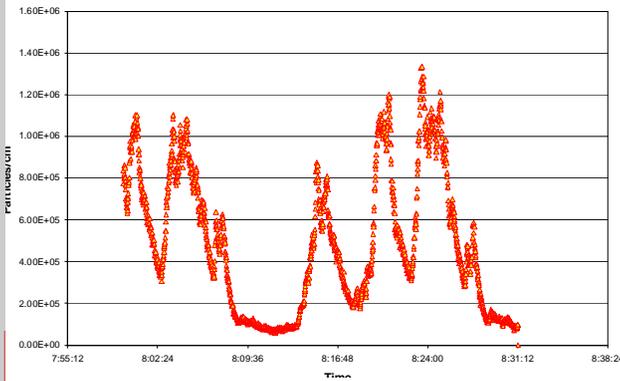
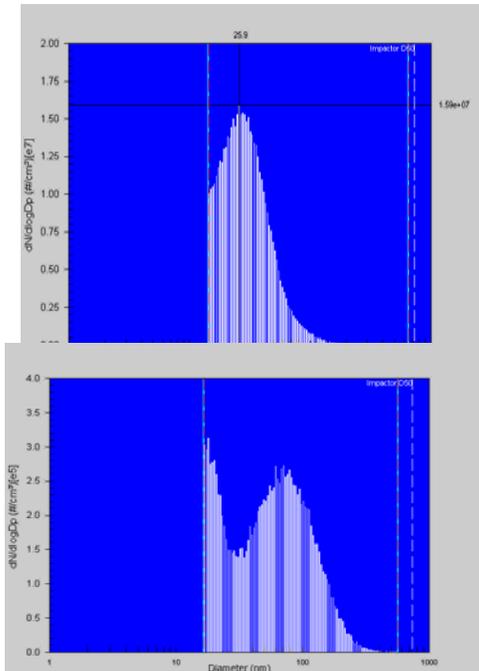
## Hardwood Smoke

PM Concentration in High Level Chamber During a 6-hr Day



### 2 Points in Cycle

### Number of 20 nm Particles/cc During One Cycle



High Burn

Low Burn



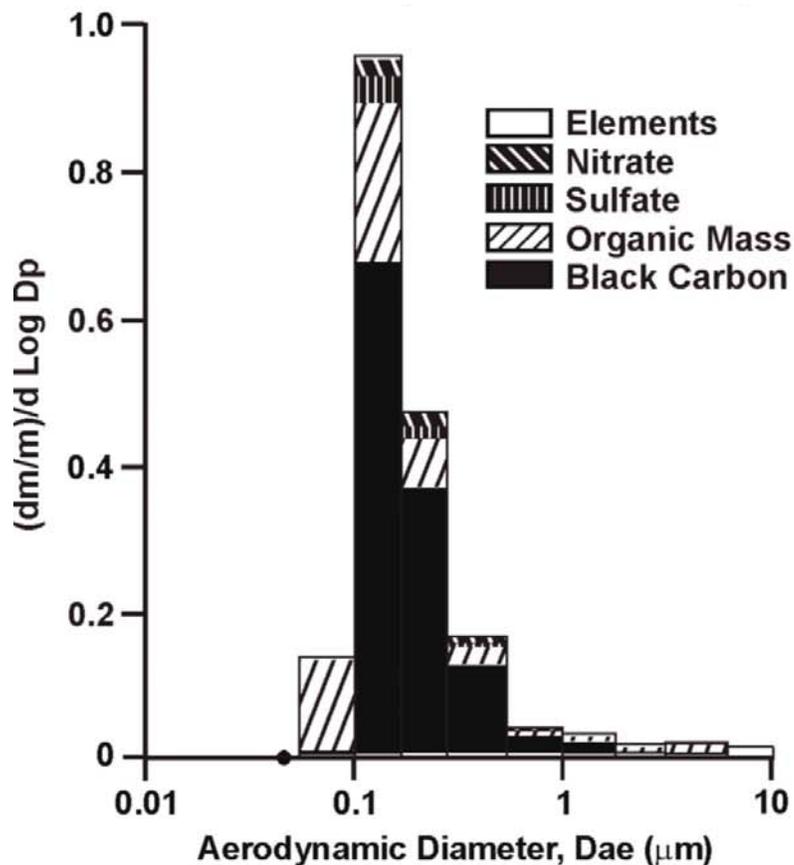
[McDonald et al., *Env. Sci. Technol.* 38: 2513, 2004]



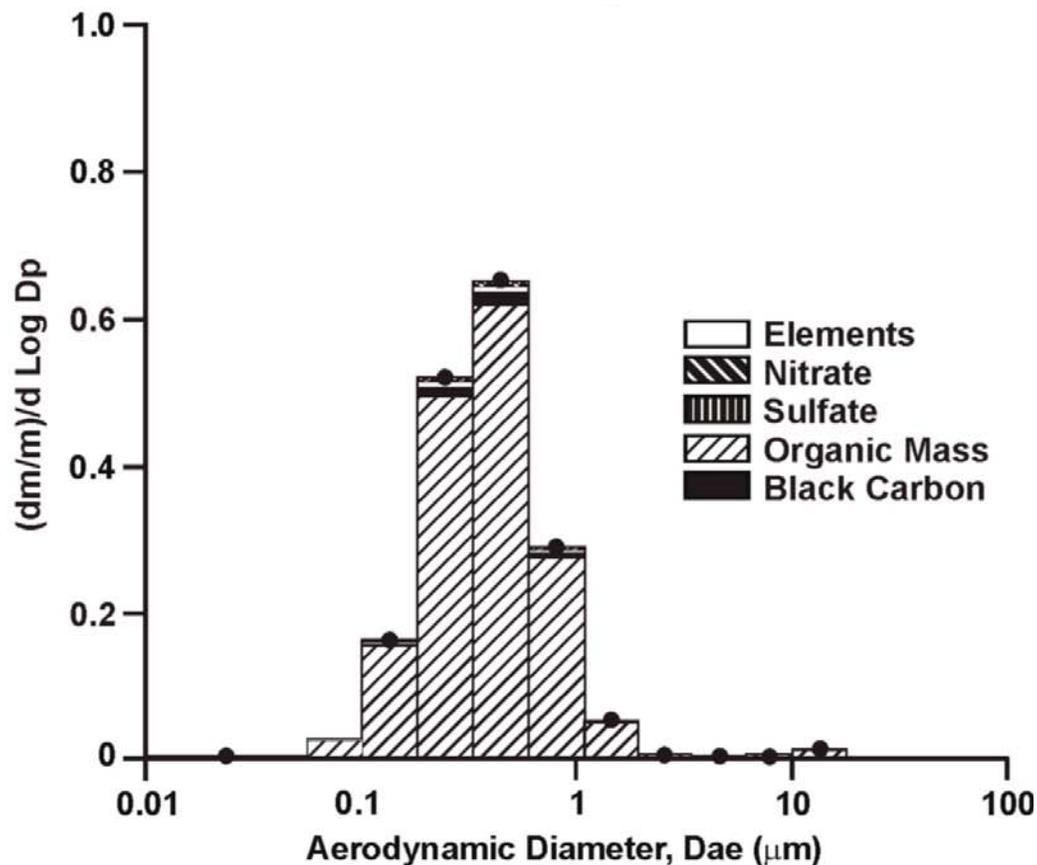
# PARTICLE MASS-SPECIFIC COMPOSITION

At High Exposure Concentration ( $1,000 \mu\text{g PM}/\text{m}^3$ )

Diesel



Hardwood Smoke

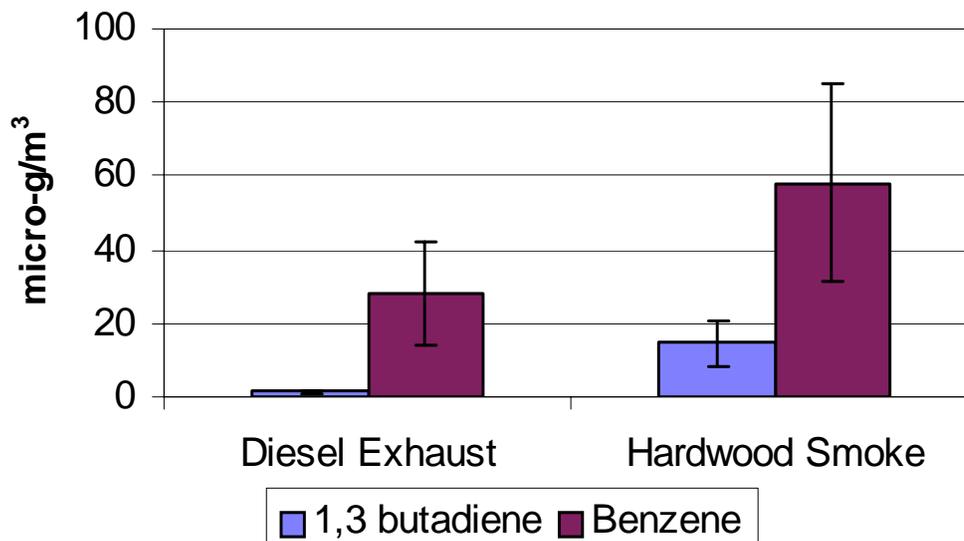


# GASES AND VAPORS

## Selected Gases (ppm)

	<u>DE</u>	<u>HWS</u>
CO	30	13
NOx	49	"0"
THC	2.2	3.1

## Selected Volatile Organics



**Therefore – comparative toxicity would depend on the exposure parameter used for comparison**

**E.g., If toxicity were identical per unit of PM mass:**

**DE would be more toxic  
per unit of PM organic  
carbon**

**HWS would be more toxic:  
per unit of PM black carbon**



# HEALTH OUTCOMES

## General toxicity in F344/CrlBR rats and A/J mice

Body & organ weights

Hematology, serum chemistry

Bronchoalveolar lavage

Histopathology

Lung gene expression

## Cardiovascular effects in SHR/Crl rats

Heart rate and variability

ECG segments

Heart and vessel histopathology

## Susceptibility to respiratory infection in C57/BL6 mice

*Pseudomonas aeruginosa*

Respiratory Syncytial Virus

## Pulmonary immune responses in BALB/C mice

Development of allergic responses

Exacerbation of allergic responses

## Carcinogenic potential in F344/CrlBR rats and A/J mice:

DNA Methylation

Oxidative DNA damage

Micronuclei

Lung adenomas in A/J mice



# **MANY HEALTH ENDPOINTS WERE NOT SIGNIFICANTLY AFFECTED BY EITHER EXPOSURE (Even at the Highest Exposure Level !!)**

**Screening criteria for “significant exposure-related effect”:**

- 1. Significant trend across all groups**
- 2. One or both highest level groups significantly different from control by multiple comparison**

**No Significant exposure-related effect on:**

**Morbidity, mortality, body weight, most organ weights**

**Clinical observations**

**Histopathology (other than ↑ alveolar macrophages with PM)**

**Most bronchoalveolar lavage parameters**

**Development of allergic responses**

**Micronuclei & lung adenomas**

***DNA methylation and oxidative injury, and lung gene microarray not yet completed***

[Reed et al., *Inhal Toxicol.* 16:177, 2004]

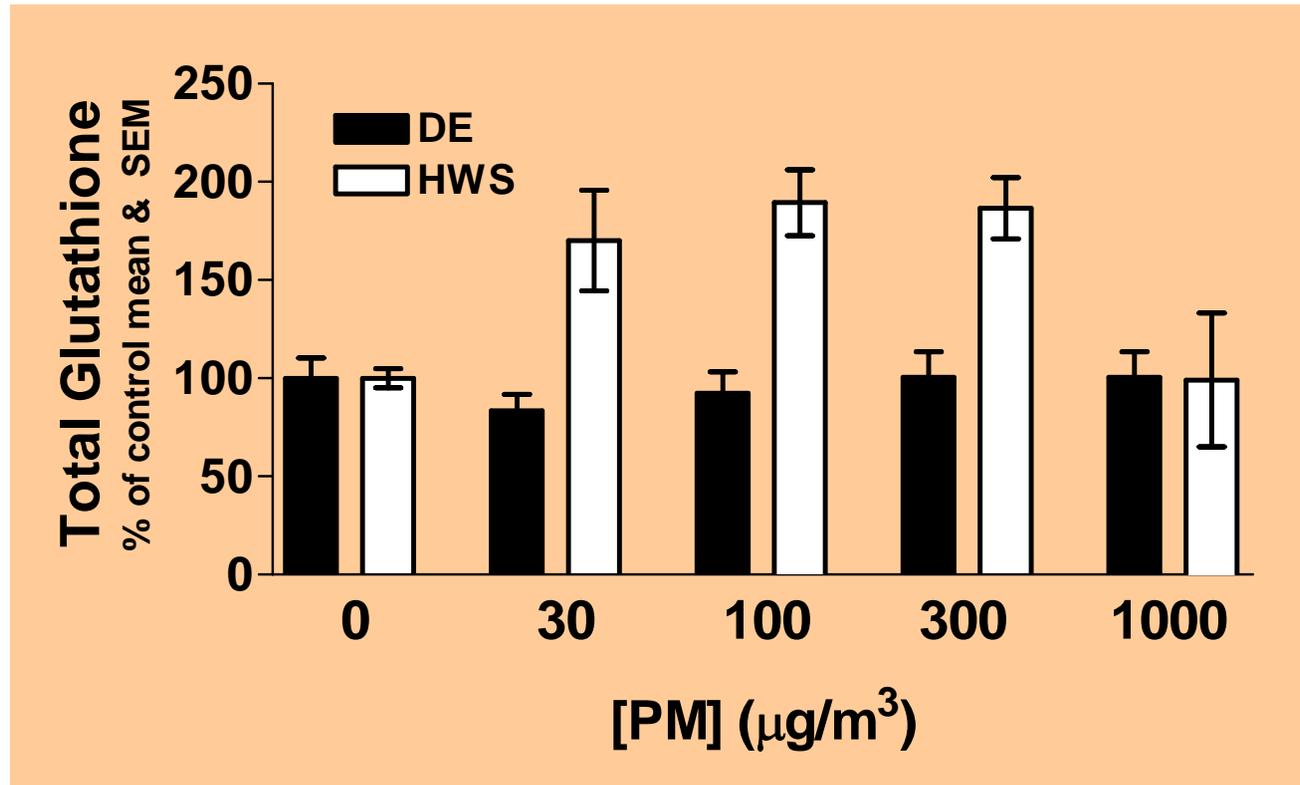
[Reed et al., *Am. J. Respir. Crit. Care Med.* 169:561, 2004]

[Seagrave et al., *Toxicologist* 78: 1380, 2004]



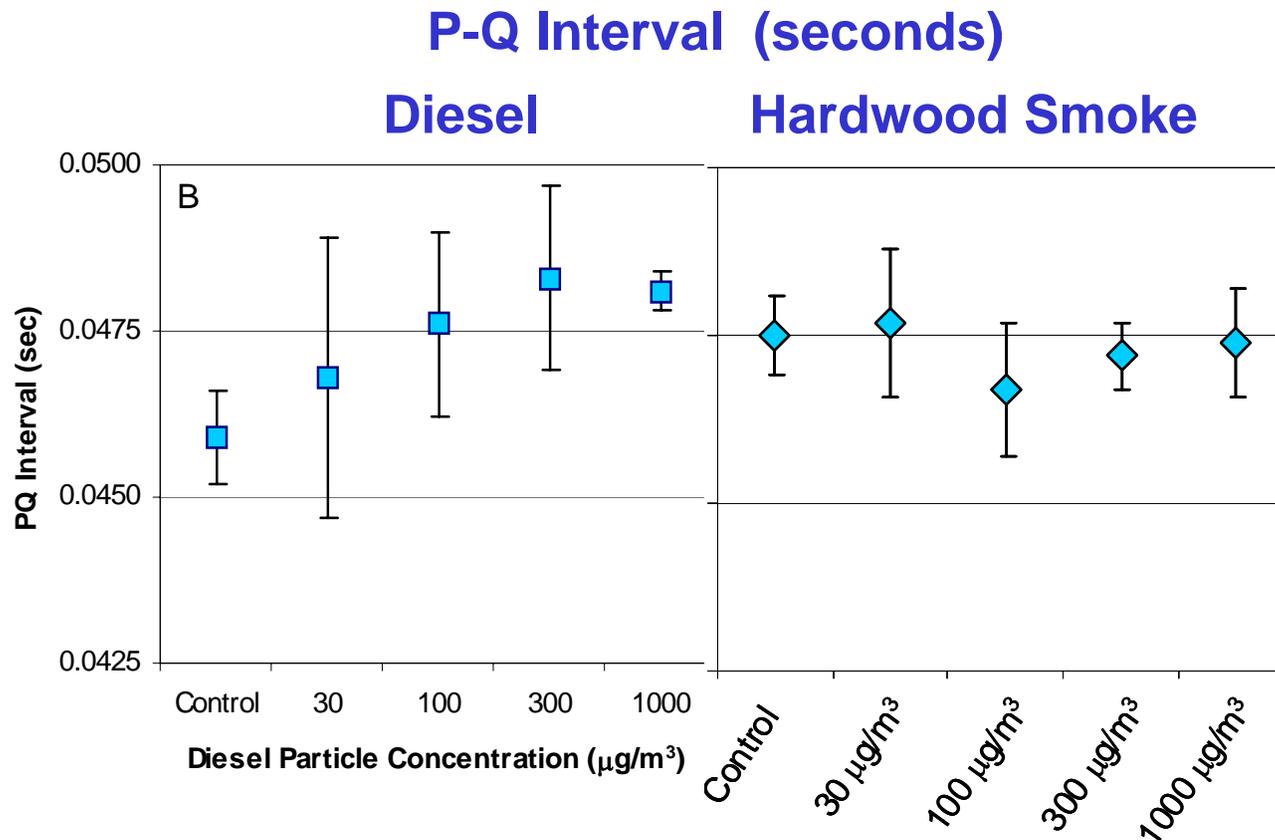
# ONLY HWS CAUSED LUNG ANTI-OXIDANT RESPONSE

Total Glutathione (reduced + oxidized)  
in Bronchoalveolar Lavage (airway) Fluid of Rats  
after 6 Months of Exposure



- HWS caused an anti-oxidant response in the lung
- DE did not

# P-Q INTERVAL OF ELECTROCARDIOGRAM WAS INCREASED BY DE BUT NOT HWS

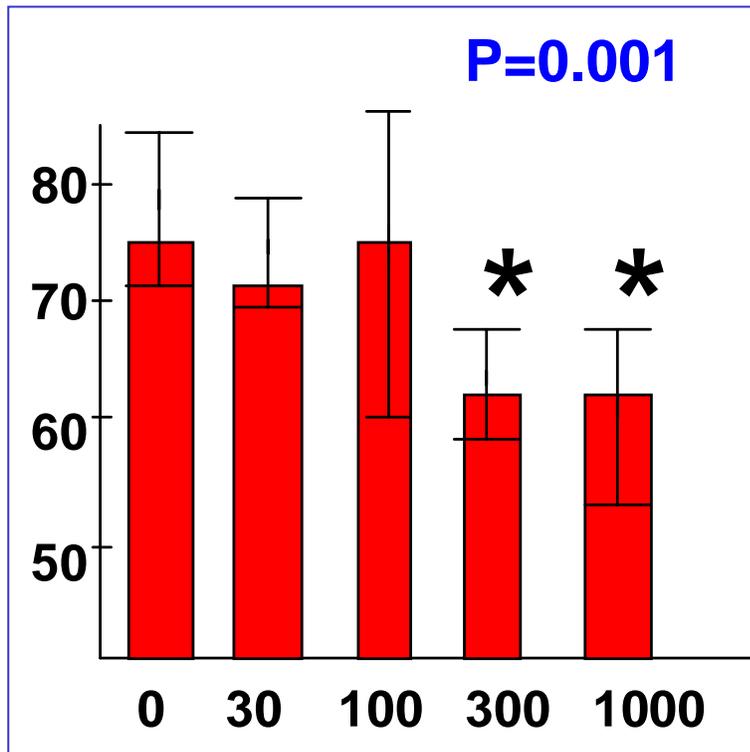


- Suggests slowing of conductivity between the atria and ventricles
- Significant only at the highest two exposure levels
- Hardwood smoke had no significant effect



# DE AND HWS HAD DIFFERENT EFFECTS ON BLOOD CLOTTING FACTORS

DE reduced Factor VII at 7 days of exposure



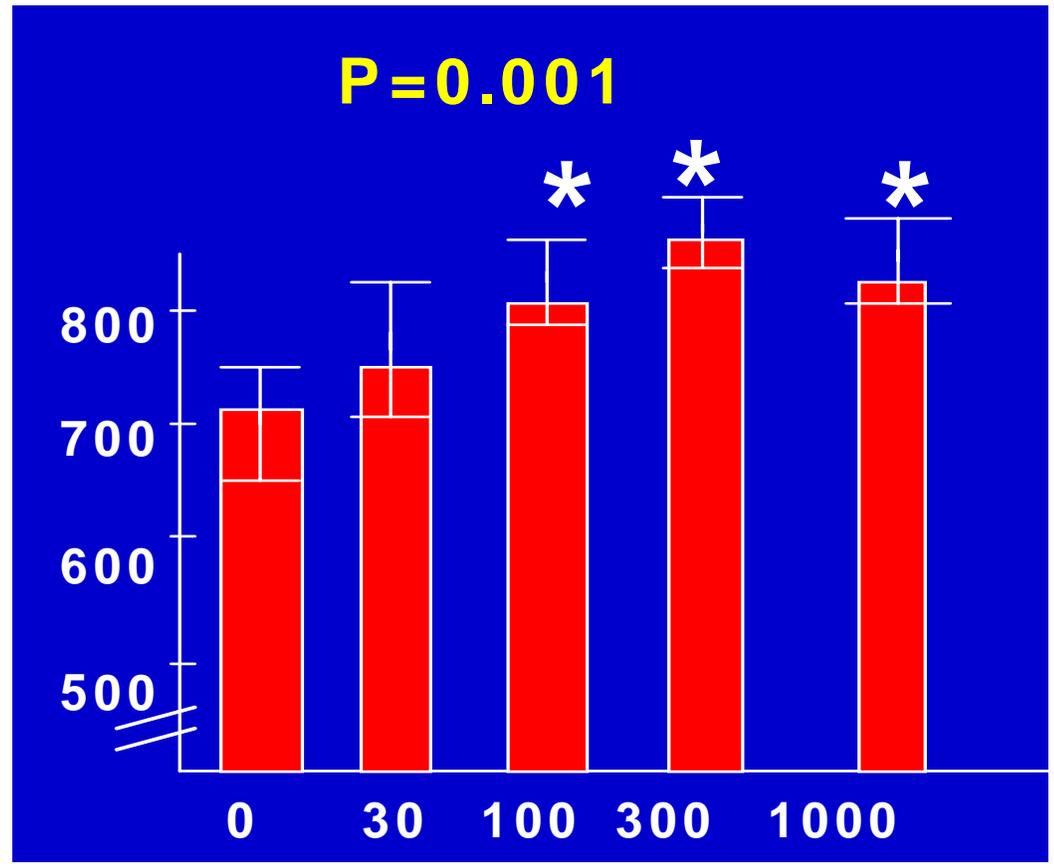
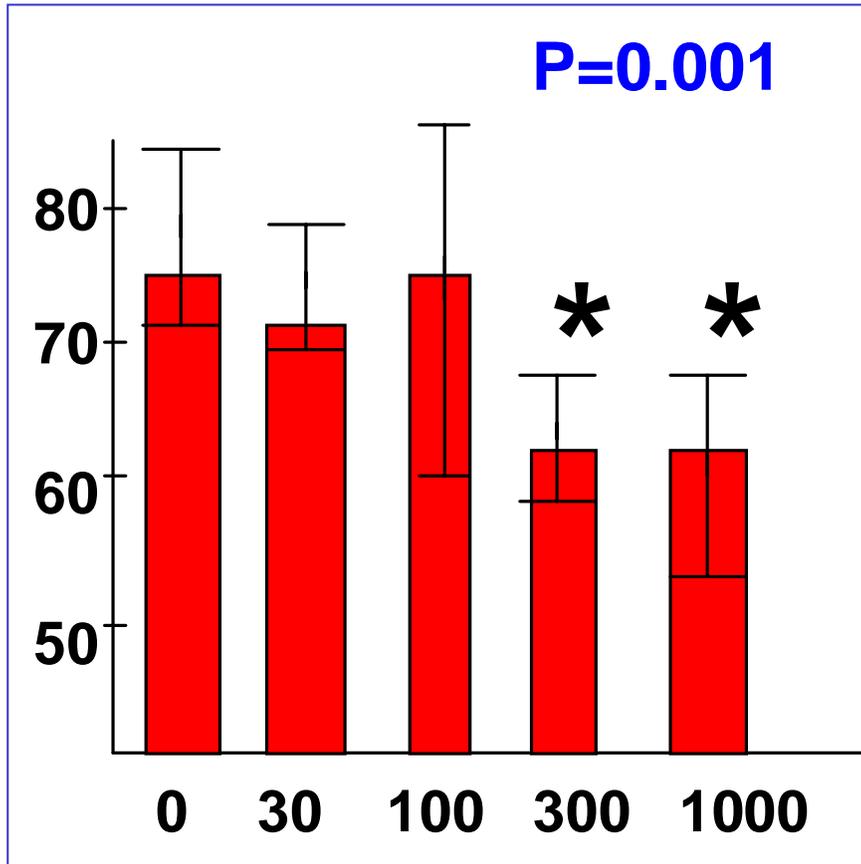
Factor VII also ↓ in humans associated with ambient PM and experimental CAPs exposure



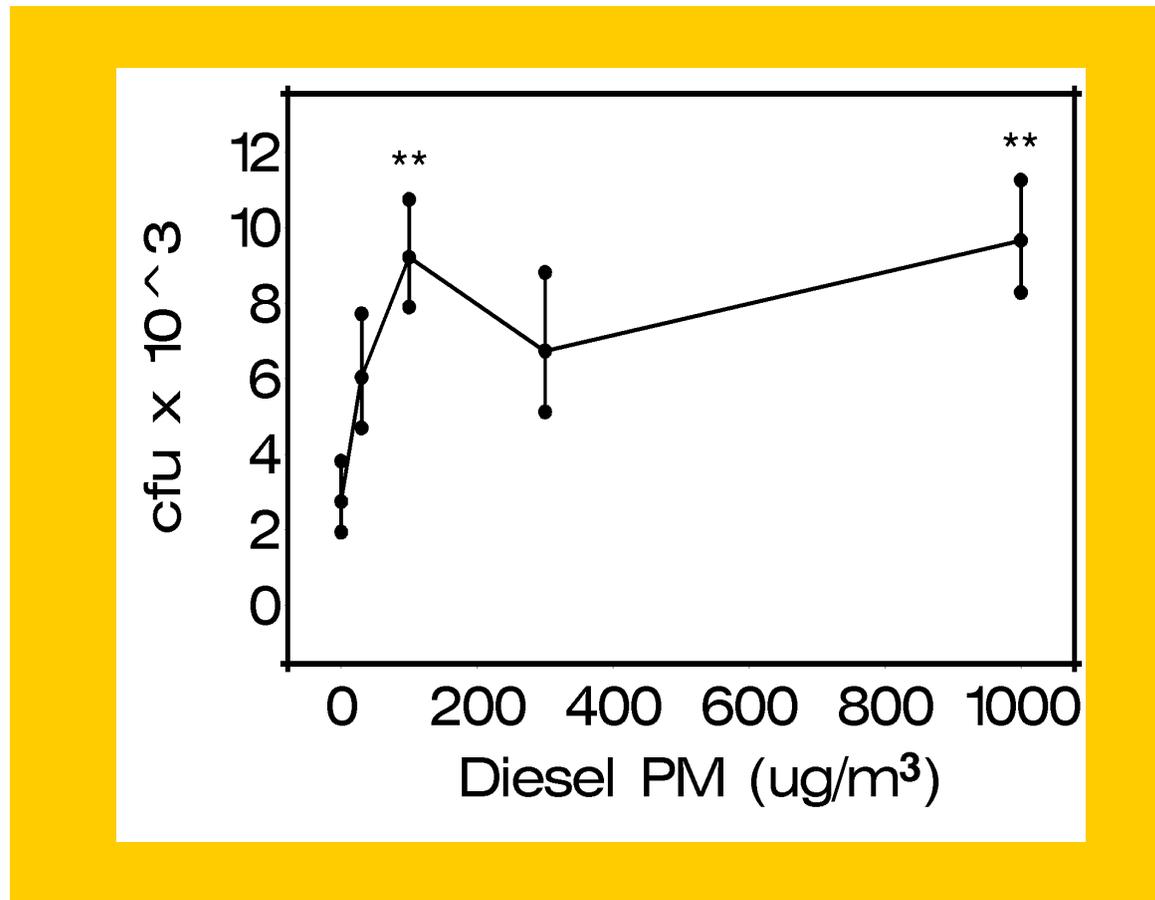
# DE AND HWS HAD DIFFERENT EFFECTS ON BLOOD CLOTTING FACTORS

DE reduced Factor VII at 7 days of exposure

HWS increased platelets at 6 months of exposure



# CLEARANCE OF BACTERIA WAS SLOWED BY DE, BUT NOT HWS



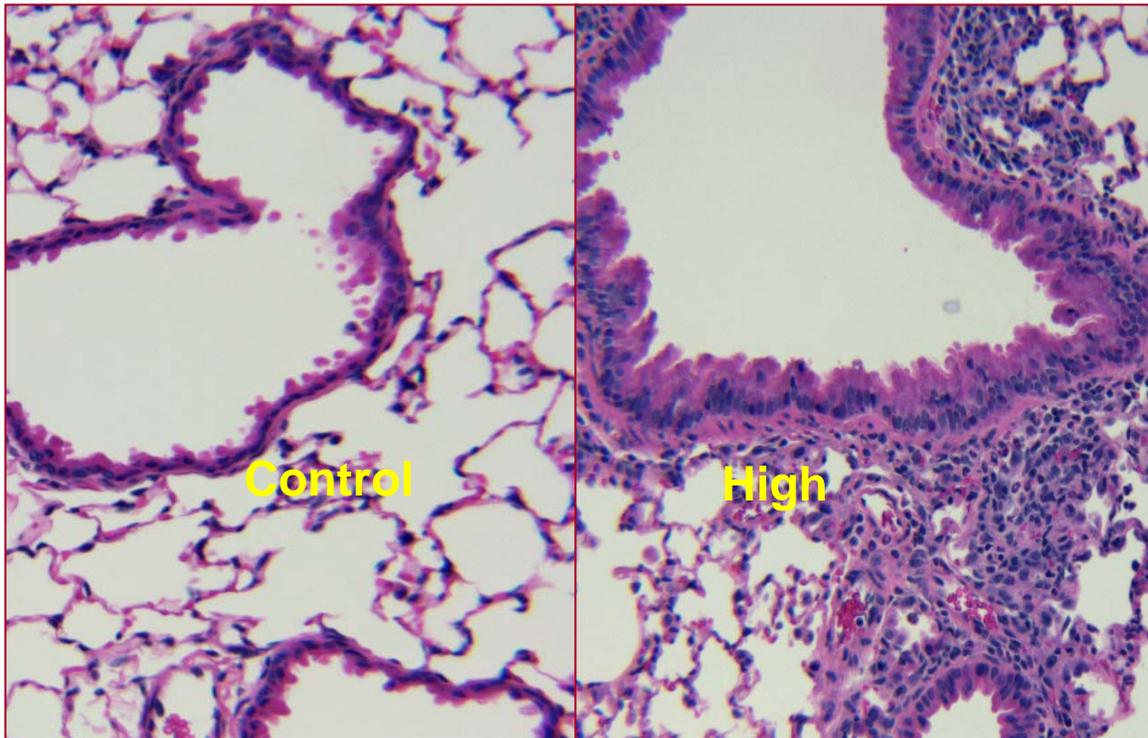
- The number of live *Pseudomonas aeruginosa* in the lung at 18 hours after infection was increased by DE
- Clearance of bacteria was not slowed by HWS



# BOTH DE AND HWS INCREASED RSV PATHOLOGY, DE ALSO SLOWED CLEARANCE OF RSV

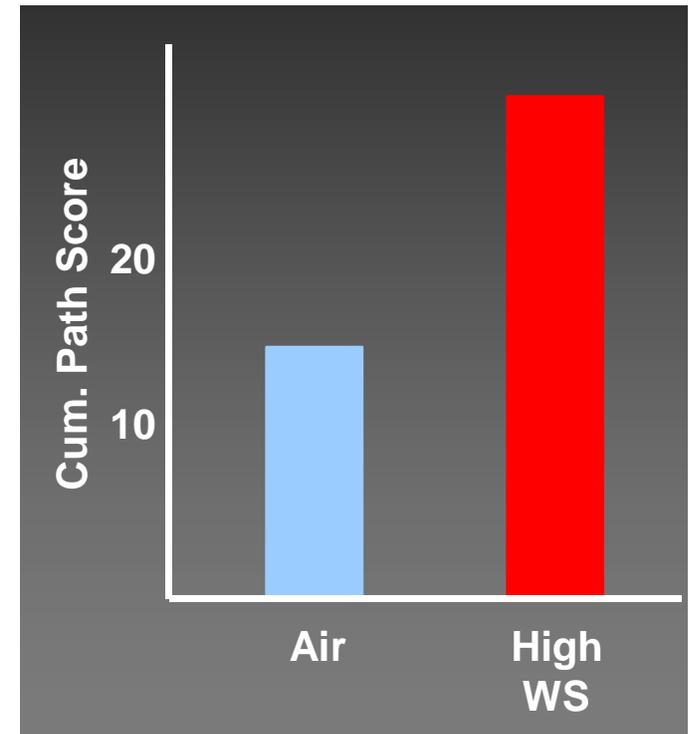
## Pathology of Small Airways

E.g., DE

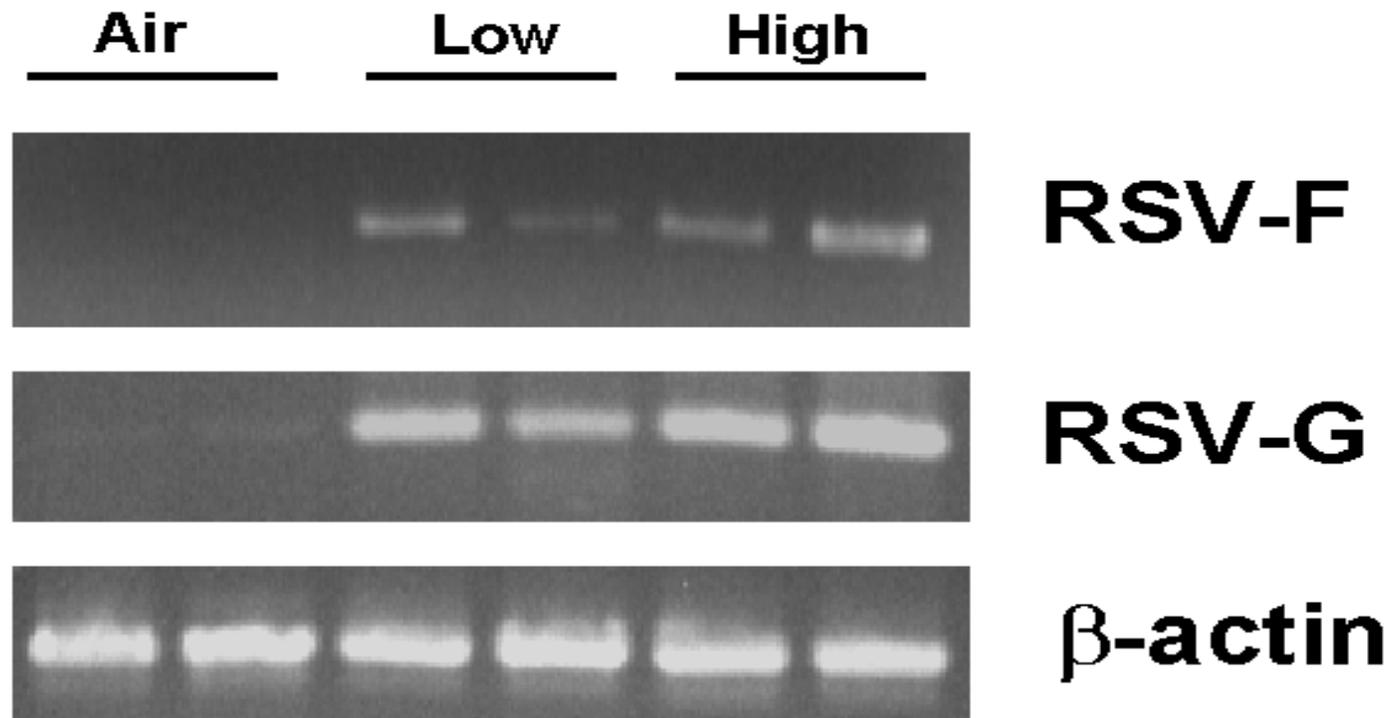


## Total Histopathology Score

E.g., HWS



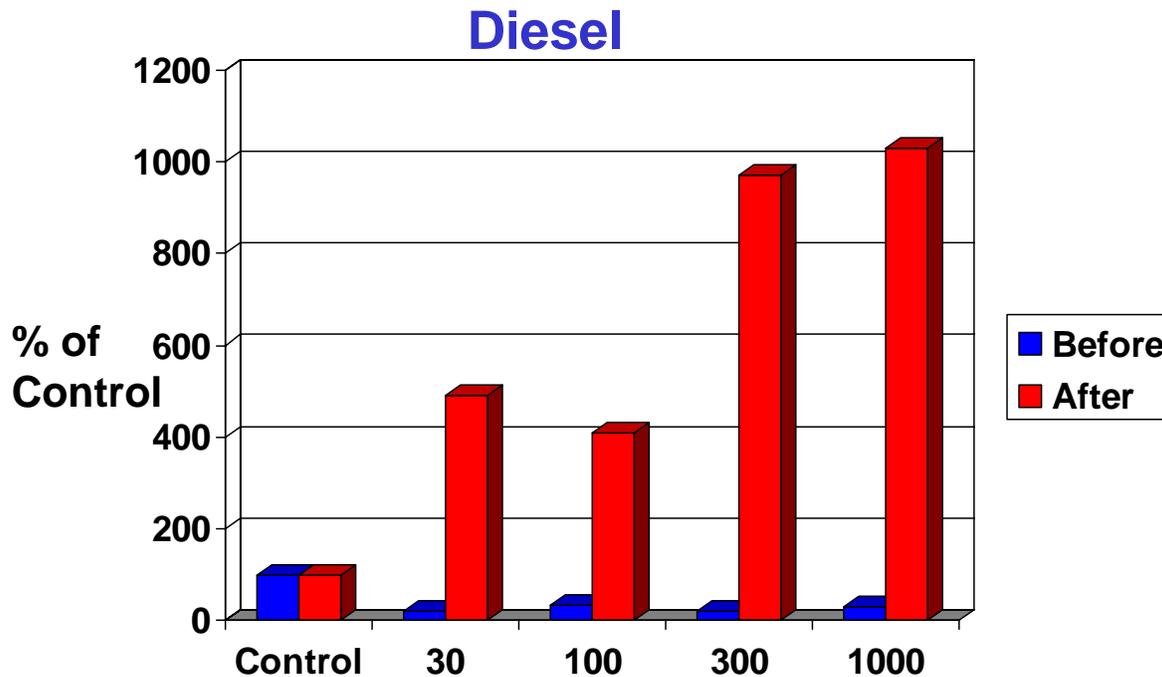
# BOTH DE AND HWS INCREASED RSV PATHOLOGY DE ALSO SLOWED CLEARANCE OF RSV



- More respiratory syncytial virus RNA was present at 4 days after infection in DE-exposed mice
- HWS did not slow clearance of RSV

# EFFECT OF EXPOSURE ON LUNG ALLERGIC RESPONSES VARIED BY BOTH EXPOSURE MATERIAL AND EXPOSURE ORDER

Effect of Exposure **Before** or **After** Allergen Challenge on Numbers of Allergic Inflammatory Cells in the Lung



- DE **before** challenge suppressed allergic response
- DE **after** challenge increased allergic response



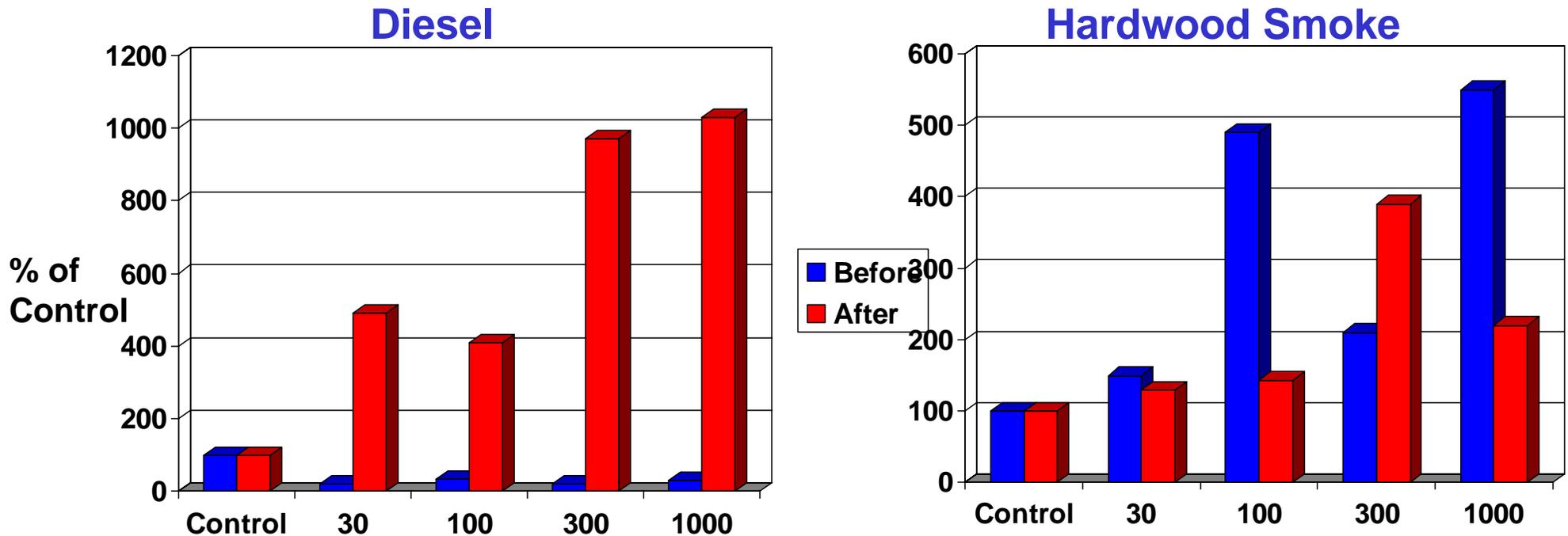
[Barrett et al., Am J Respir. Crit. Care Med. 169: 652, 2004]

[Barrett et al., Am. J. Physiol. Lung Cell Mol. Physiol, in press]



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Effect of Exposure **Before** or **After** Allergen Challenge on Numbers of Allergic Inflammatory Cells in the Lung



- DE **before** challenge suppressed allergic response
- DE **after** challenge increased allergic response
- HWS tended to increase allergic response in either sequence

[Barrett et al., Am J Respir. Crit. Care Med. 169: 652, 2004]

[Barrett et al., Am. J. Physiol. Lung Cell Mol. Physiol, in press]



# BOTTOM LINES

You can't understand risk unless you understand the doses necessary to cause effects

Everything is toxic at some exposure level

You can't understand relative risk unless you make direct comparisons

You can't compare data collected using different methods

Effects of diesel emissions and wood smoke differ... *(duh)* ... but relative risk depends on the exposure metric

There is no single "correct" metric  
(except perhaps risk per unit of work)

Our goal is to identify physical-chemical species that cause important effects - so they can be reduced or avoided

We are taking multiple approaches to the problem