

Human Clinical Studies of Ultrafine Particles

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Air Pollution and Hospital Readmissions of MI Survivors

von Klot et al. Circulation 2005

TABLE 3. Pooled Results of Poisson Regressions of the Association of Hospital Readmissions and Same-Day Air Pollution Concentrations

Pollutant	Unit	Hospital Readmissions, RR (95% CI)		
		Myocardial Infarction	Angina Pectoris	Cardiac*
PNC	10 000/cm ³	1.039 (0.998–1.082)†	1.020 (0.992–1.048)	1.026 (1.005–1.048)
PM ₁₀	10 μg/m ³	1.026 (0.995–1.058)	1.008 (0.986–1.032)	1.021 (1.004–1.039)
CO	0.2 mg/m ³ (0.172 ppm)	1.022 (0.998–1.047)	1.009 (0.992–1.026)	1.014 (1.001–1.026)
NO ₂	8 μg/m ³ (4.16 ppb)	1.028 (0.997–1.060)	1.032 (1.006–1.058)	1.032 (1.014–1.051)
O ₃ ‡	15 μg/m ³ (7.5 ppb)	1.000 (0.954–1.048)	1.044 (1.012–1.077)	1.026 (1.001–1.051)

*Hospital admissions for acute myocardial infarction, angina pectoris, dysrhythmia, or heart failure.

†Random-effects model.

‡Daily maximum 8-hour average.

Do UFP Contribute to PM-Related Cardiovascular Disease?

- Why might UFP be important in CV disease?
 - UFP deposition in the respiratory tract
 - Human clinical studies of carbon UFP
- 

Ultrafine Particles

- UFP: <100 nm
- High surface area
- Evade macrophage phagocytosis
- Predicted high pulmonary deposition
- May enter lung interstitium and blood

Fractional Deposition of Inhaled Particles in the Human Respiratory Tract

(ICRP Model, 1994; Nose-breathing)

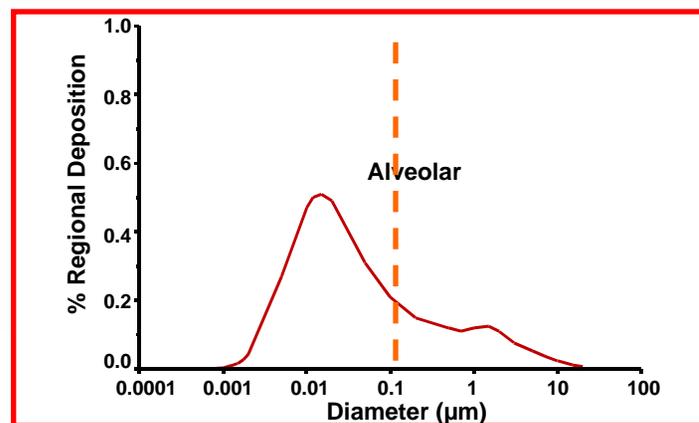
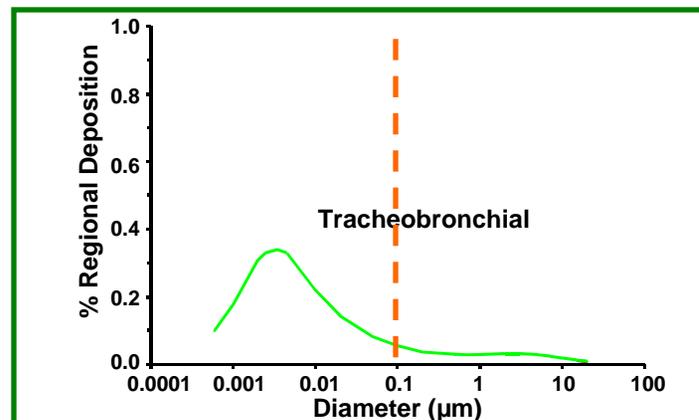
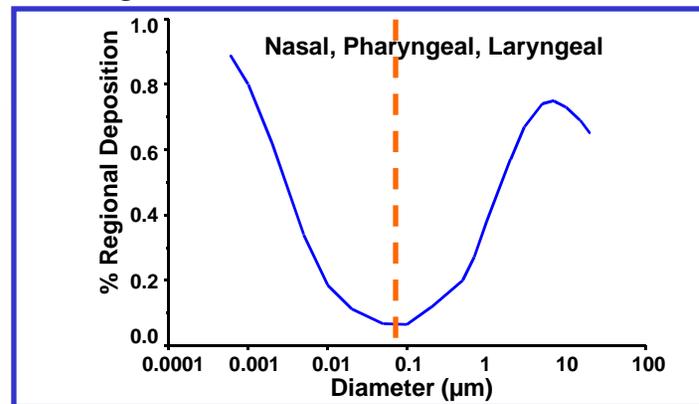
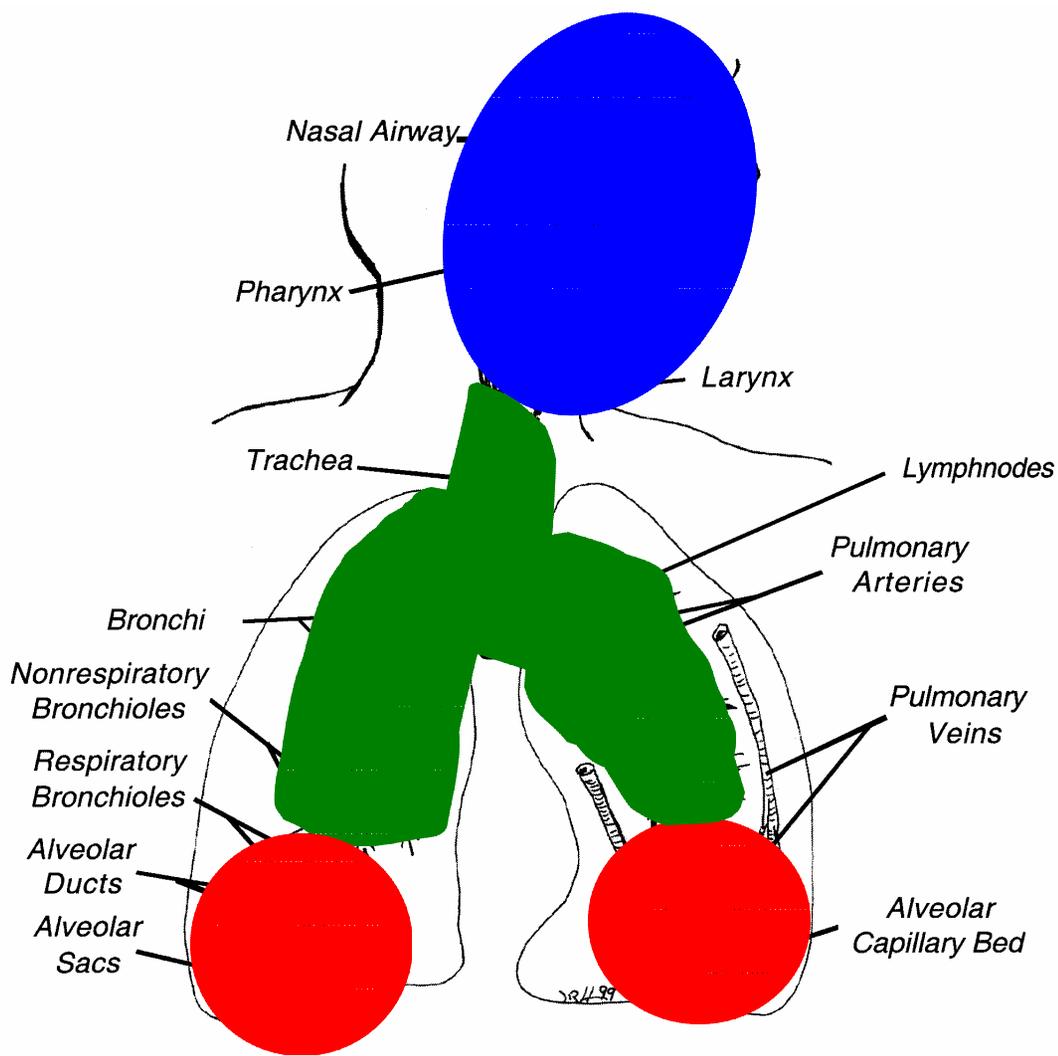
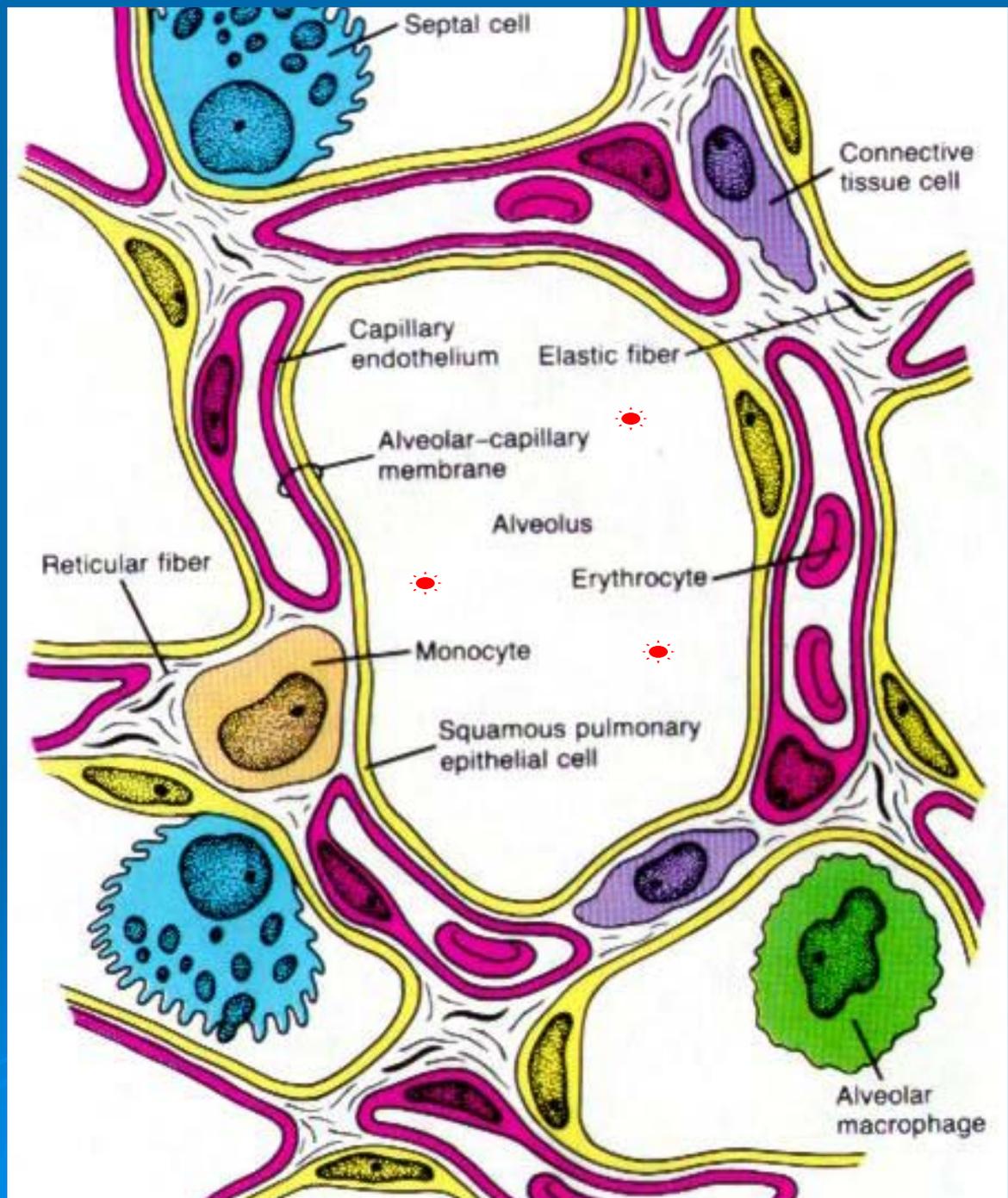


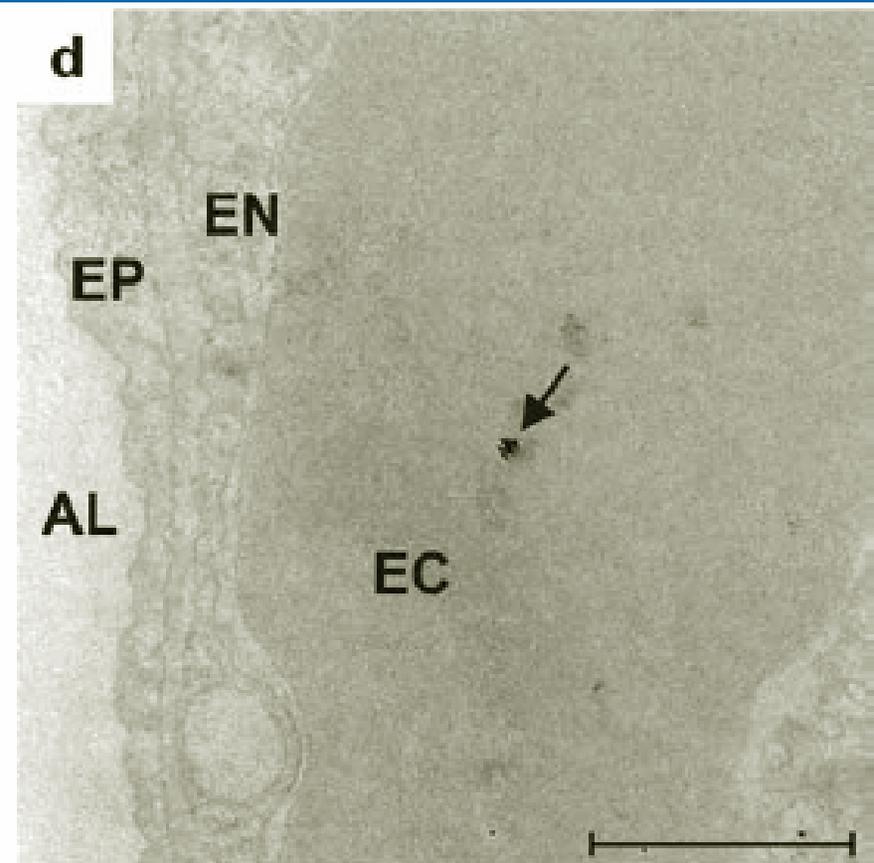
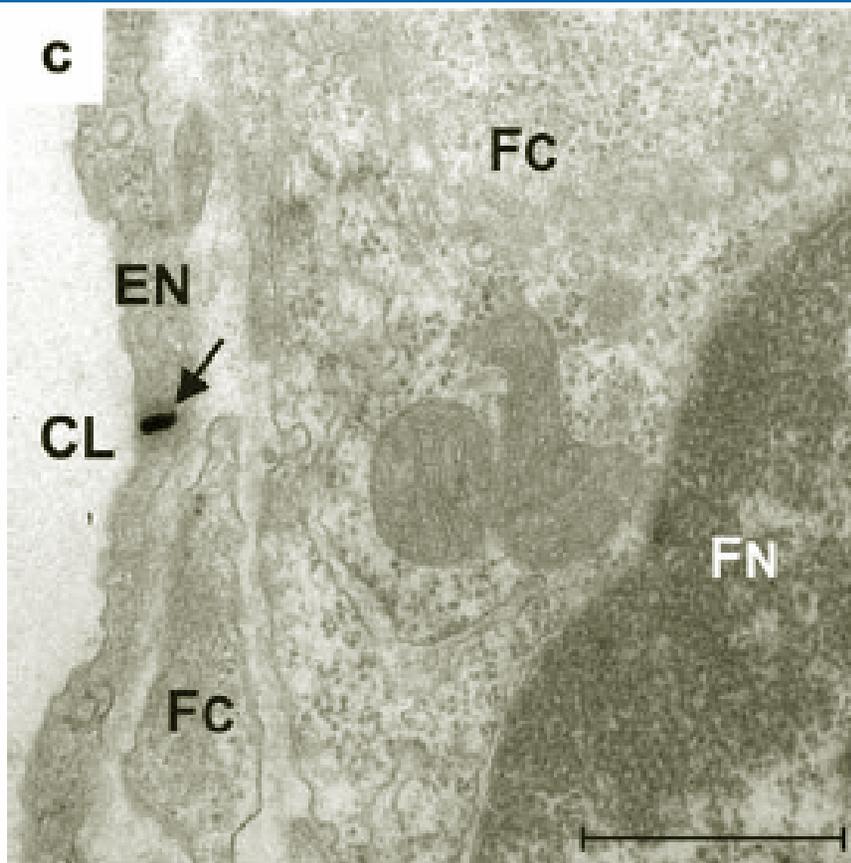
Figure courtesy of J.Harkema

Pulmonary Capillaries



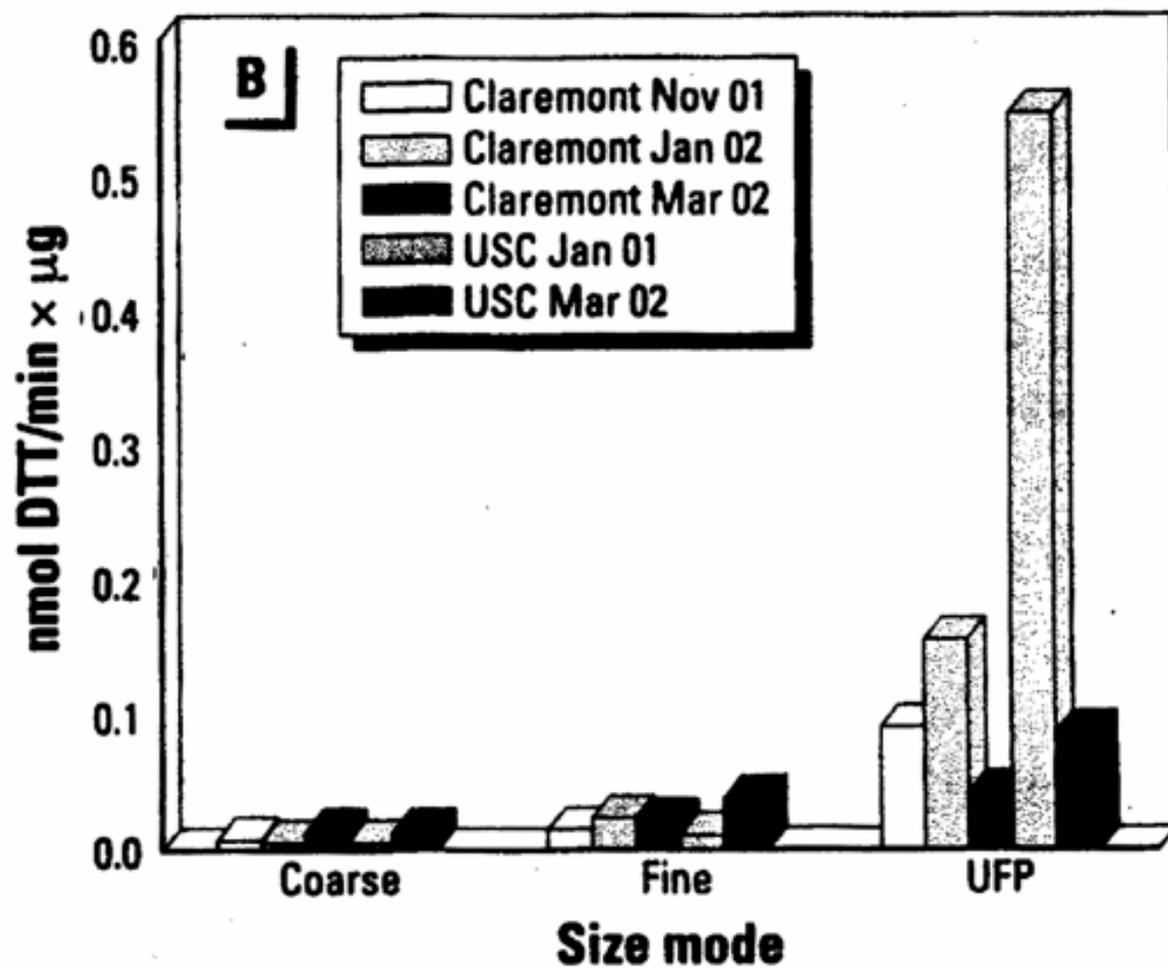
UFP Beyond the Airways

Geiser et al., EHP 2005



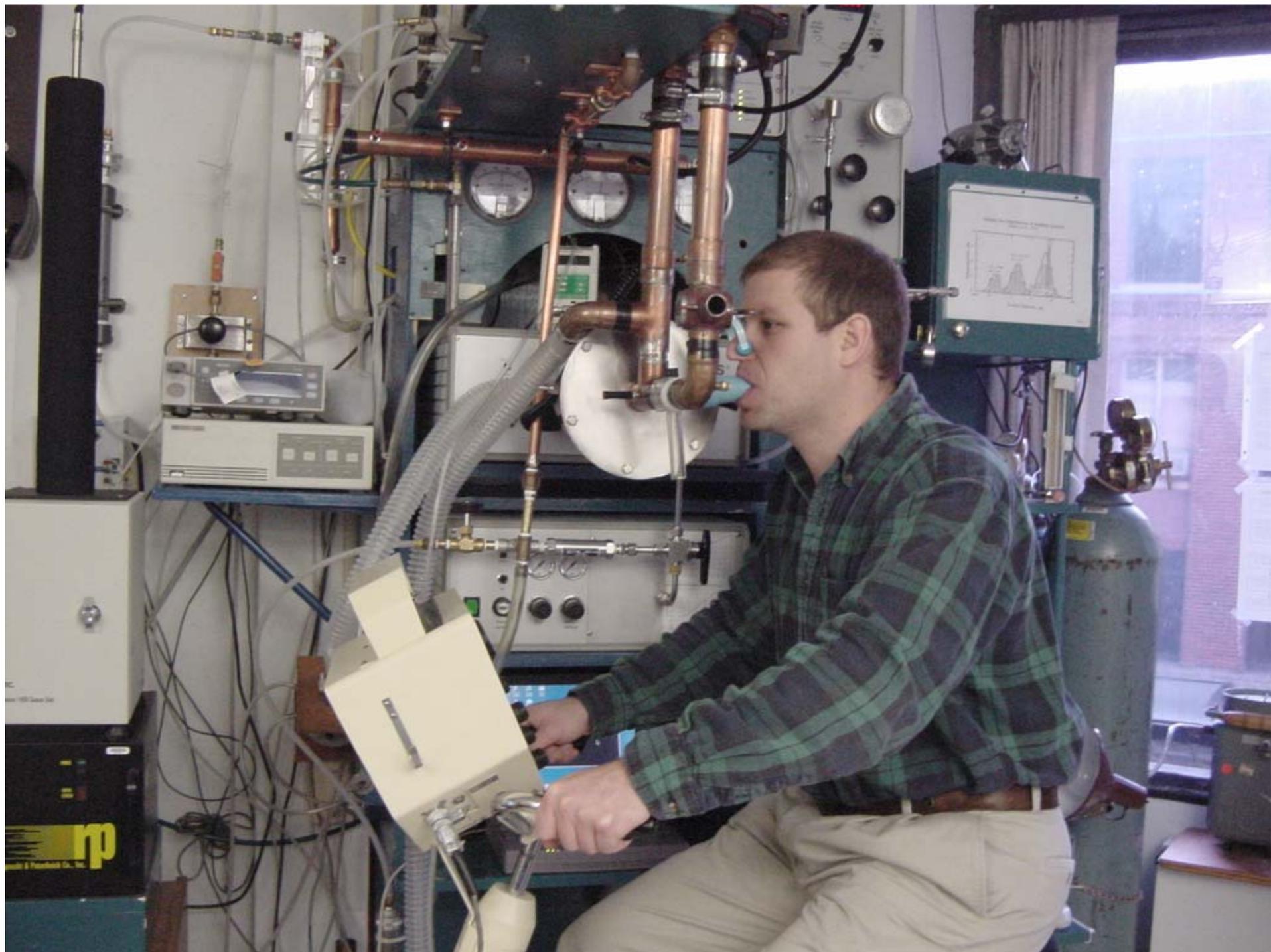
Ambient Ultrafine Particles Have Oxidant Activity

Li et al., Environ Health Perspect 2003



Question: Does UFP exposure affect the circulation?

- Pulmonary vs Systemic
 - Implications for cardiac outcomes
- 



Experimental Protocol

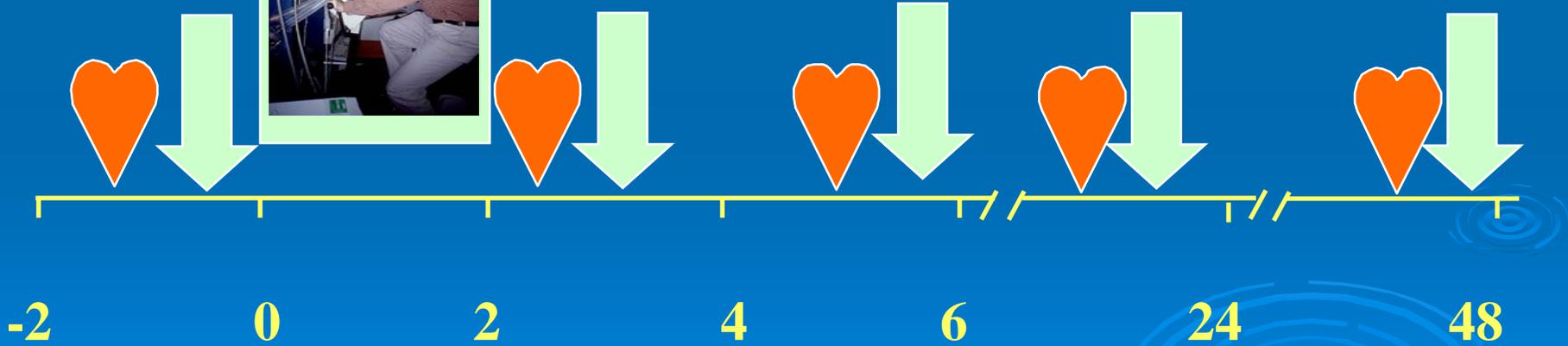
UFP or
Air



=
Symptoms
Phlebotomy
Exhaled NO
DLCO
Spirometry
Oximetry

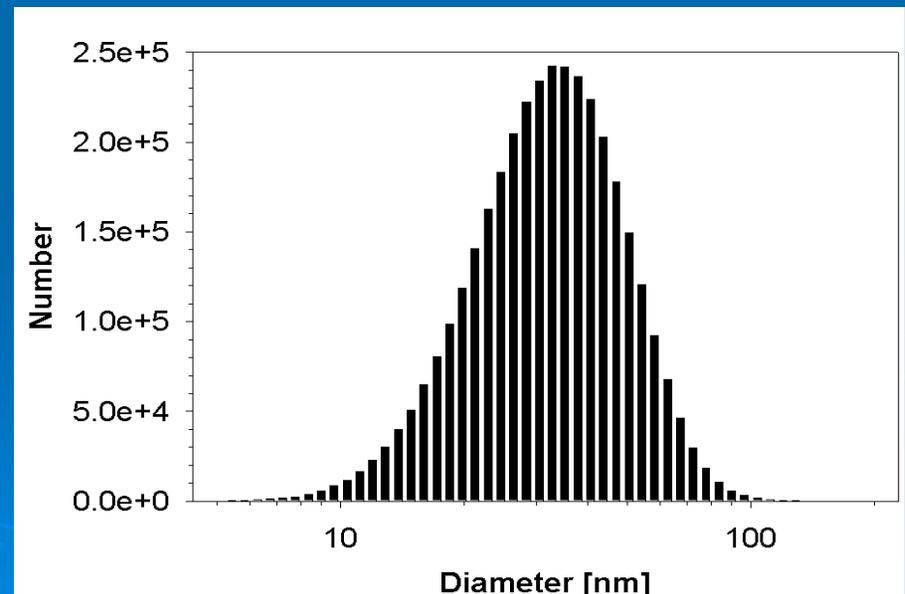


=
Resting HRV
Flow-mediated
dilatation

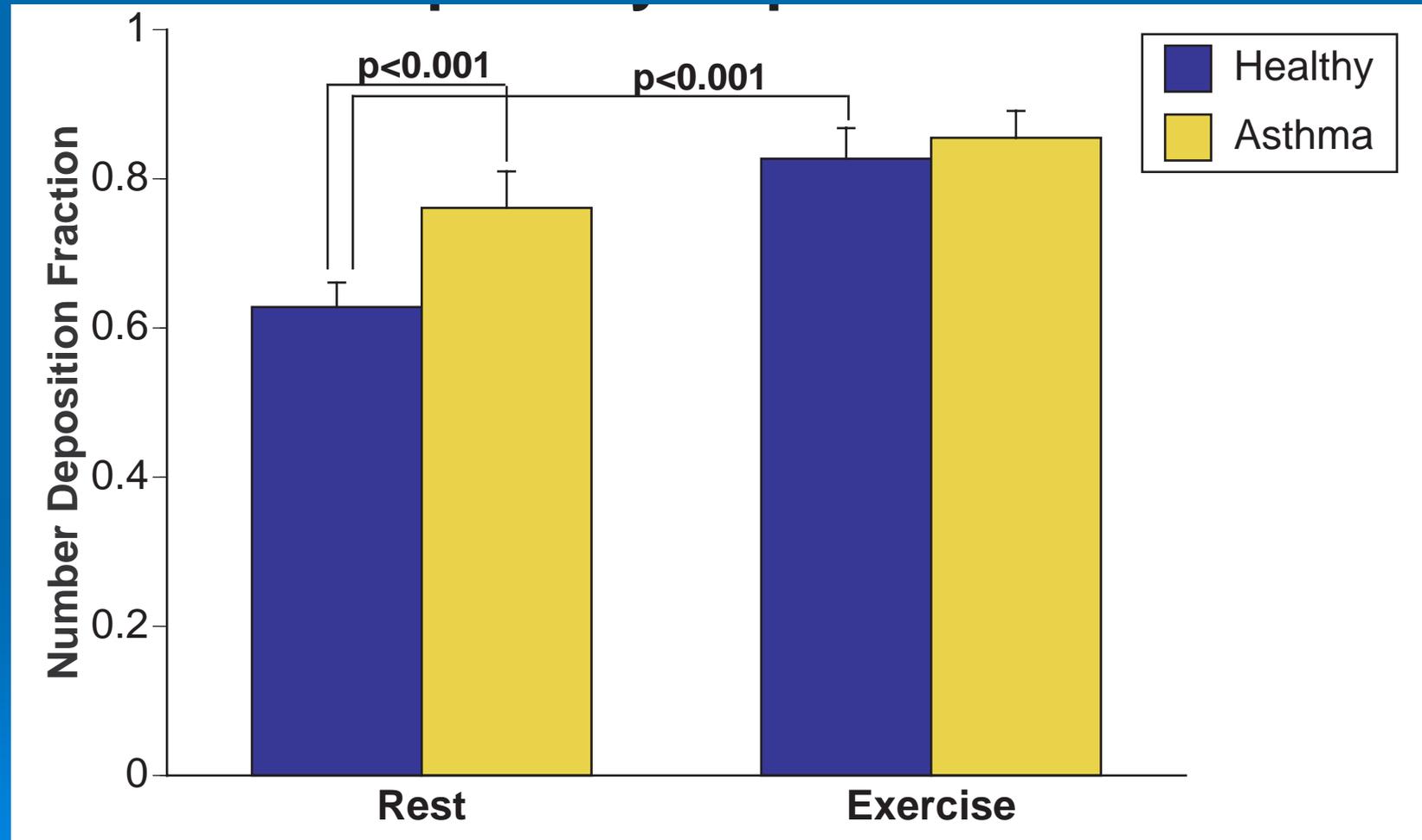


Exposure to Carbon UFP

- Count median diameter ~26 nm, GSD ~1.6
- 2 hrs by mouthpiece
- Intermittent exercise



Respiratory Deposition of UFP



Effects of Ultrafine Particles 10 to 50 $\mu\text{g}/\text{m}^3$ for 2 hr

No effects on:

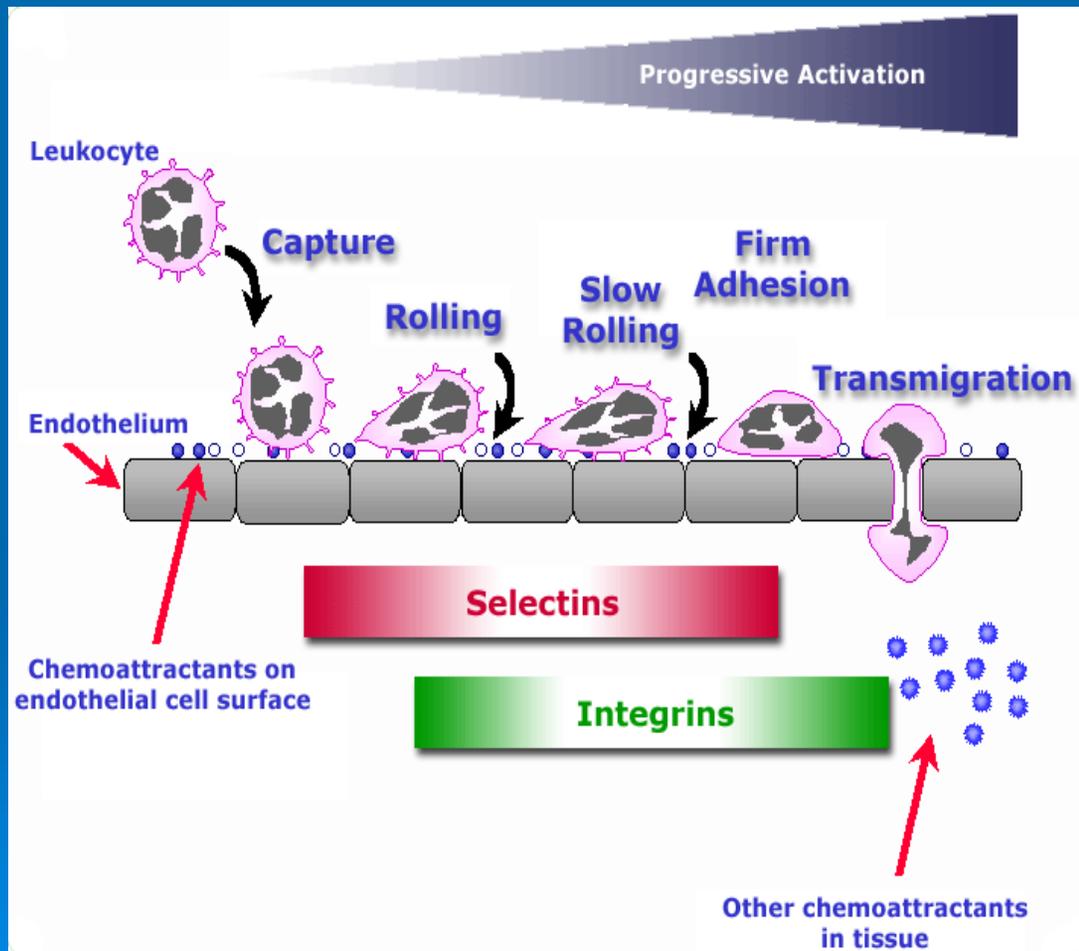
- Symptoms
- Lung function
- Airway inflammation
- Soluble markers of inflammation
- Cardiac rhythm, ST segment of ECG

A noninvasive marker of pulmonary
vascular effects:

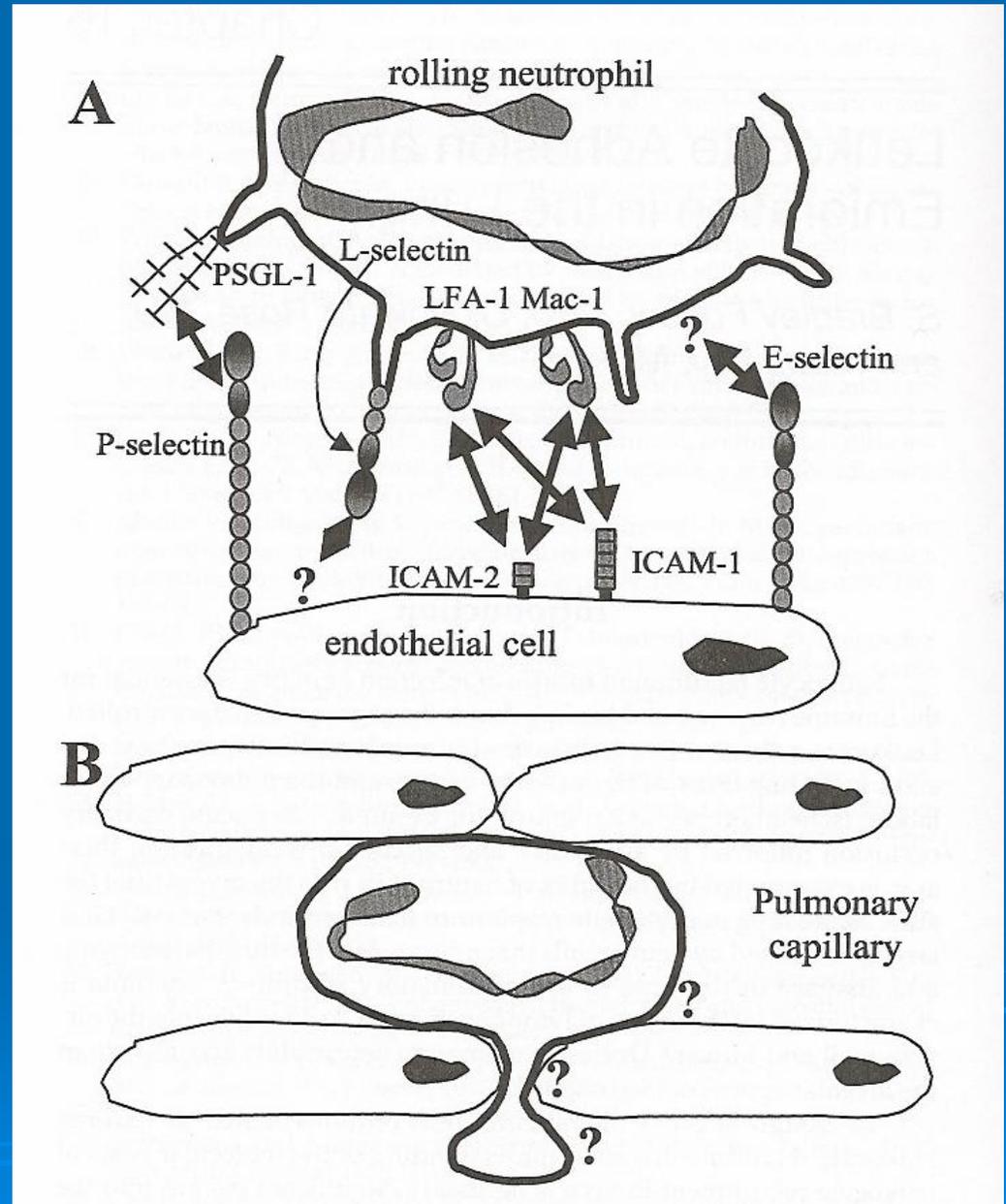
blood leukocyte expression of
adhesion molecules



Leukocyte Recruitment in Inflammation



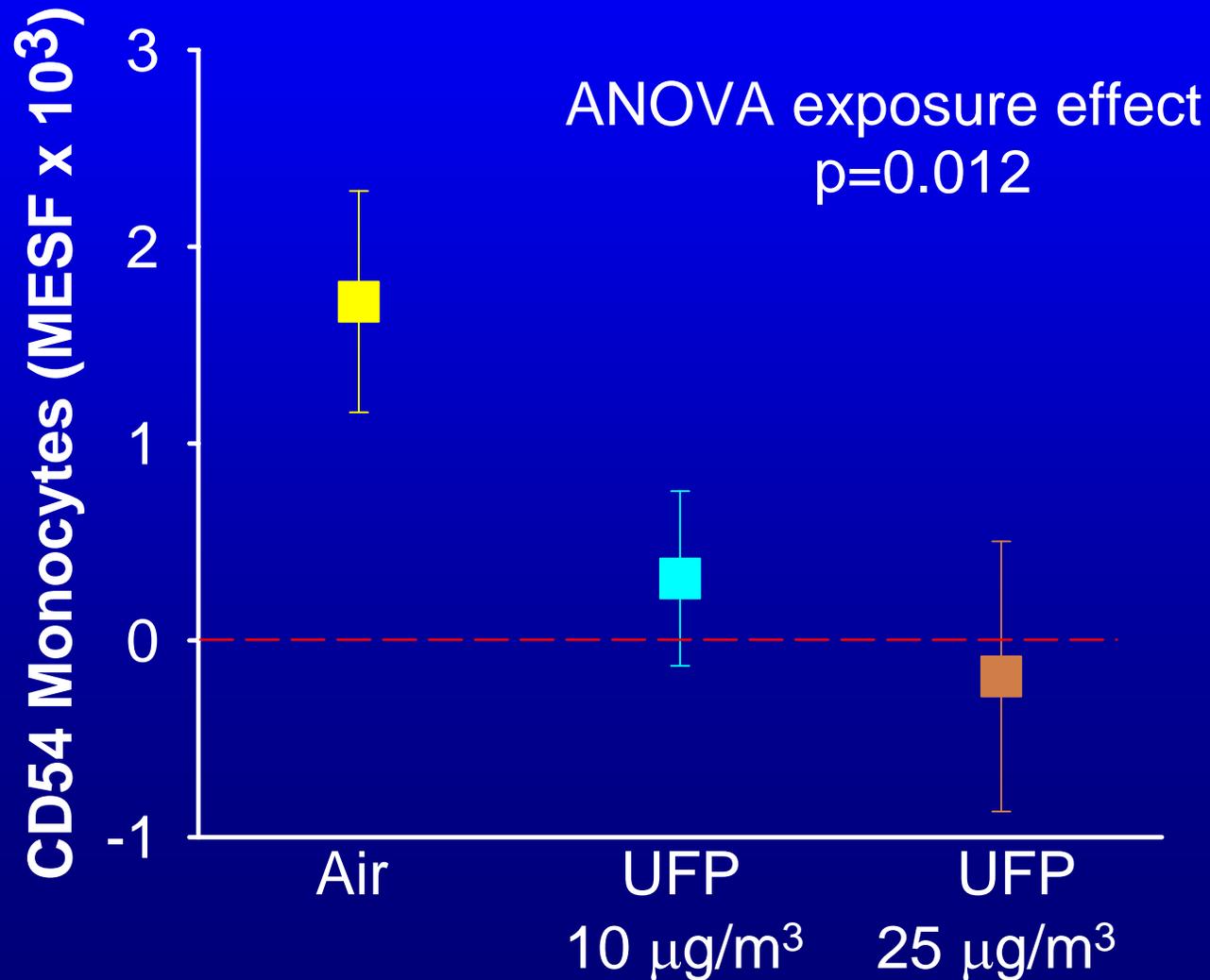
Blood Leukocytes: Markers of Vascular Events



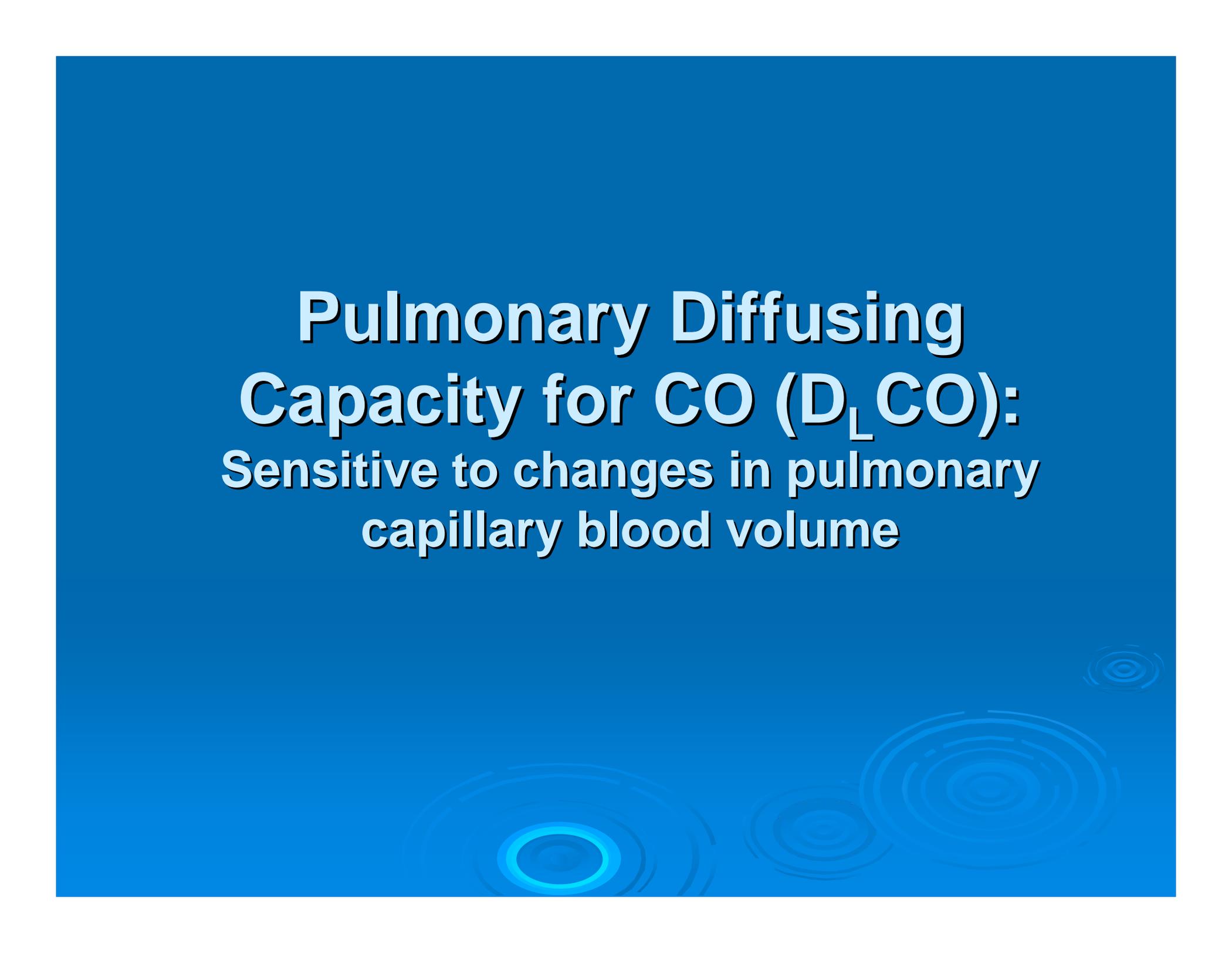
Interactions of Blood and the Pulmonary Circulation, 2002

Change in Monocyte ICAM-1 Expression 3.5 h after Exposure

Frampton et al., Environ Health Persp 2006



**Pulmonary Diffusing
Capacity for CO (D_LCO):
Sensitive to changes in pulmonary
capillary blood volume**



Hypothesis:

Pulmonary vascular effects of PM--a function of particle size and surface area?

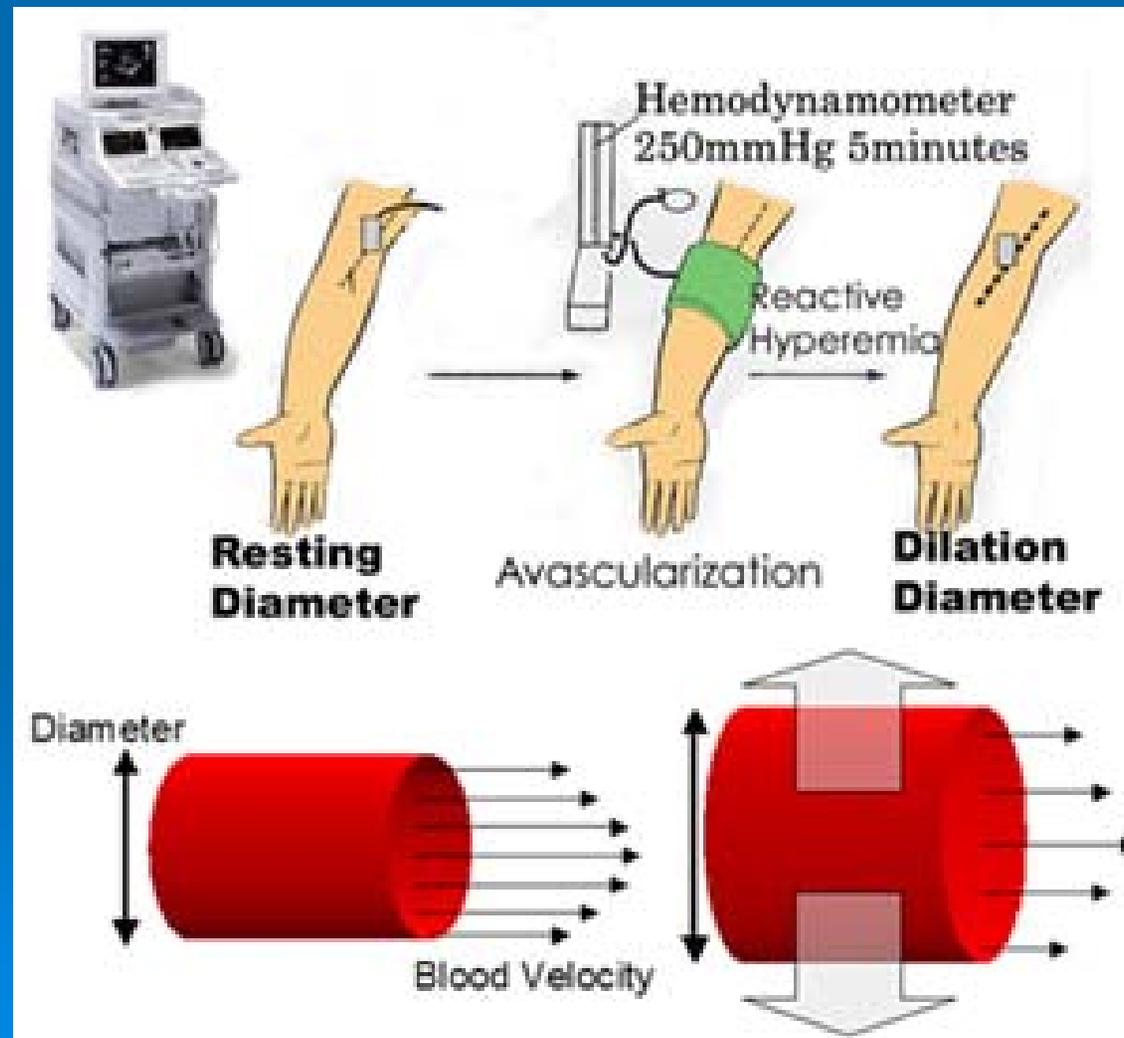
	Mass ($\mu\text{g}/\text{m}^3$)	Number (particles/ cm^3)	Count Median Diameter (nm)	GSD	Surface Area m^2/g
UFP	55 ± 2.8	$9.8 \times 10^6 \pm 1.3$	32 ± 1.2	1.63 ± 0.02	750
FP	114 ± 20.9	867 ± 155	292 ± 23.7	1.71 ± 0.05	7

Conclusion: Carbon UFP exposure may alter pulmonary vascular endothelial function in healthy subjects.

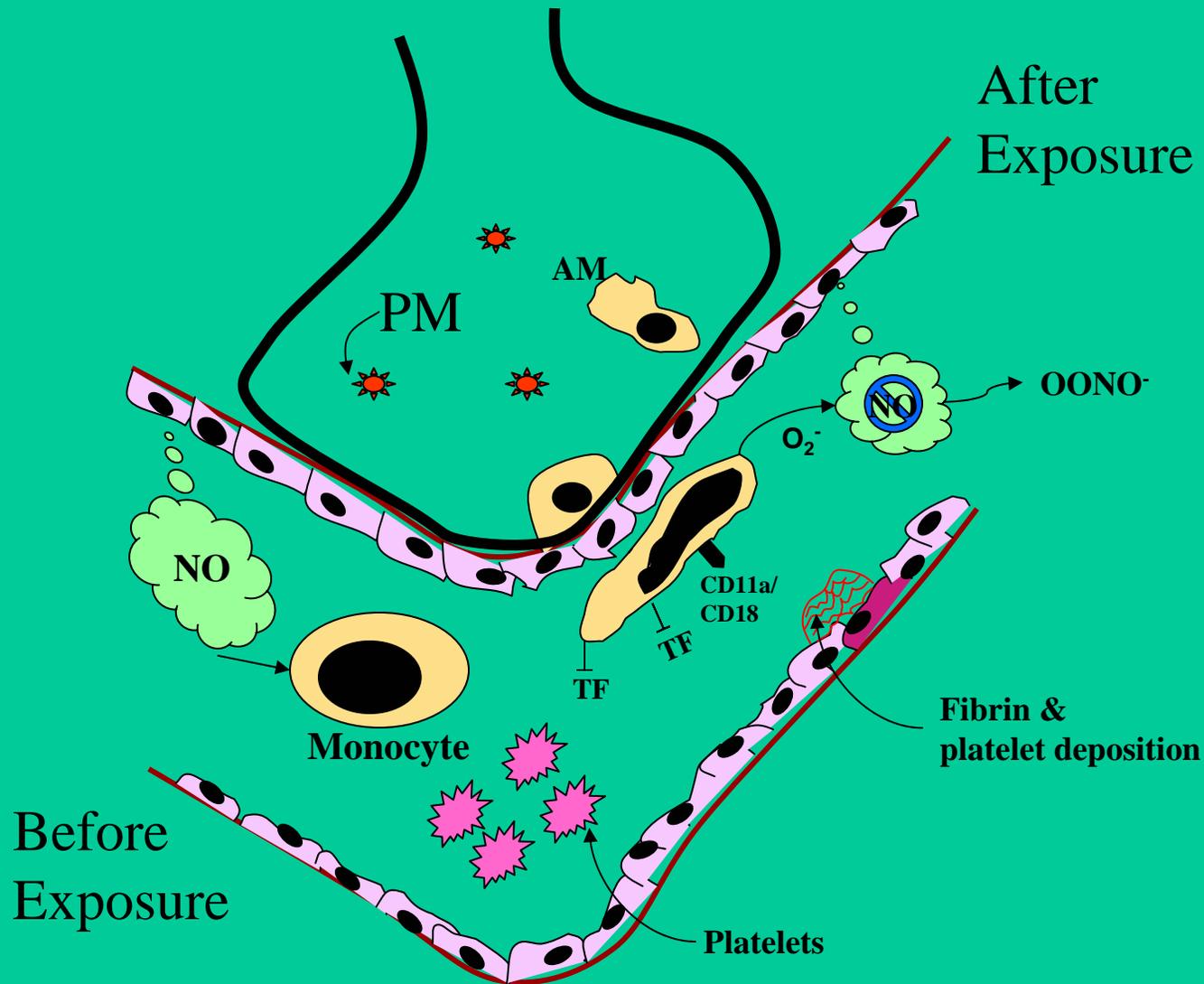
Does exposure to UFP alter systemic endothelial function?



Systemic Endothelial Function: Forearm Flow-Mediated Dilatation



Proposed UFP Vascular Effects



Summary & Speculation

- UFP fractional deposition high, increases with exercise and asthma
- UFP may impair pulmonary & systemic endothelial function
- Effects on endothelial function may underlie diverse cardiovascular effects
- Likely role for reactive oxygen species & NO
- Relative absence of airway effects
- Vascular effects of ambient UFP may be greater

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