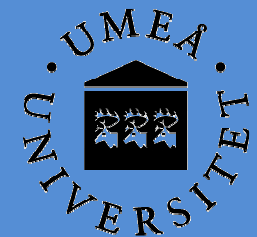




# Health Effects of Diesel Exhaust

Thomas Sandström



Beijing



London Dec. 1952



Brussels



Santiago de Chile



Umeå 2010

Sydney



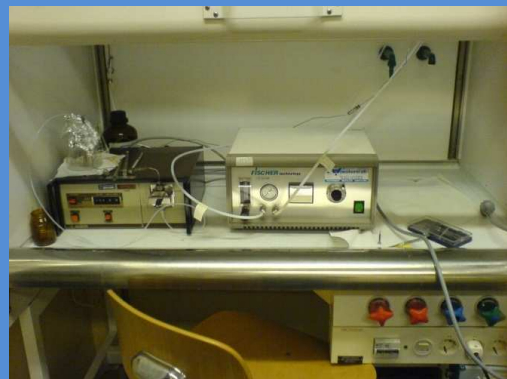
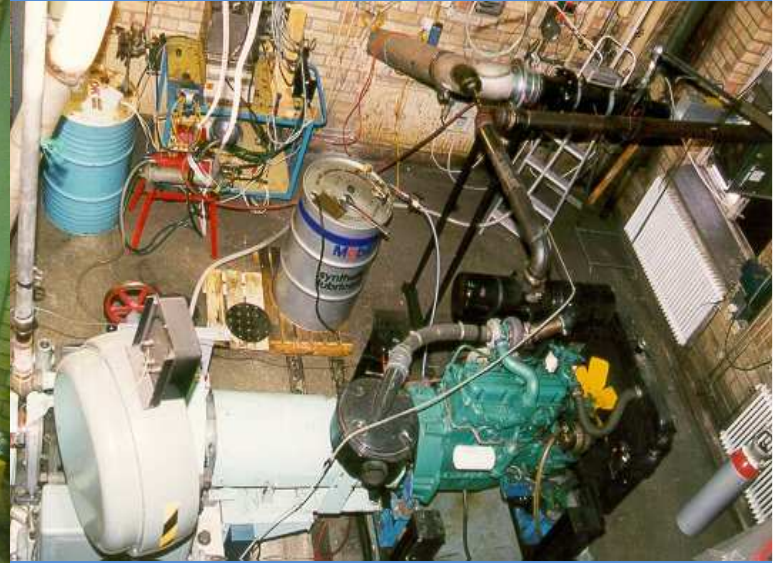
New York



London



# Chamber exposure



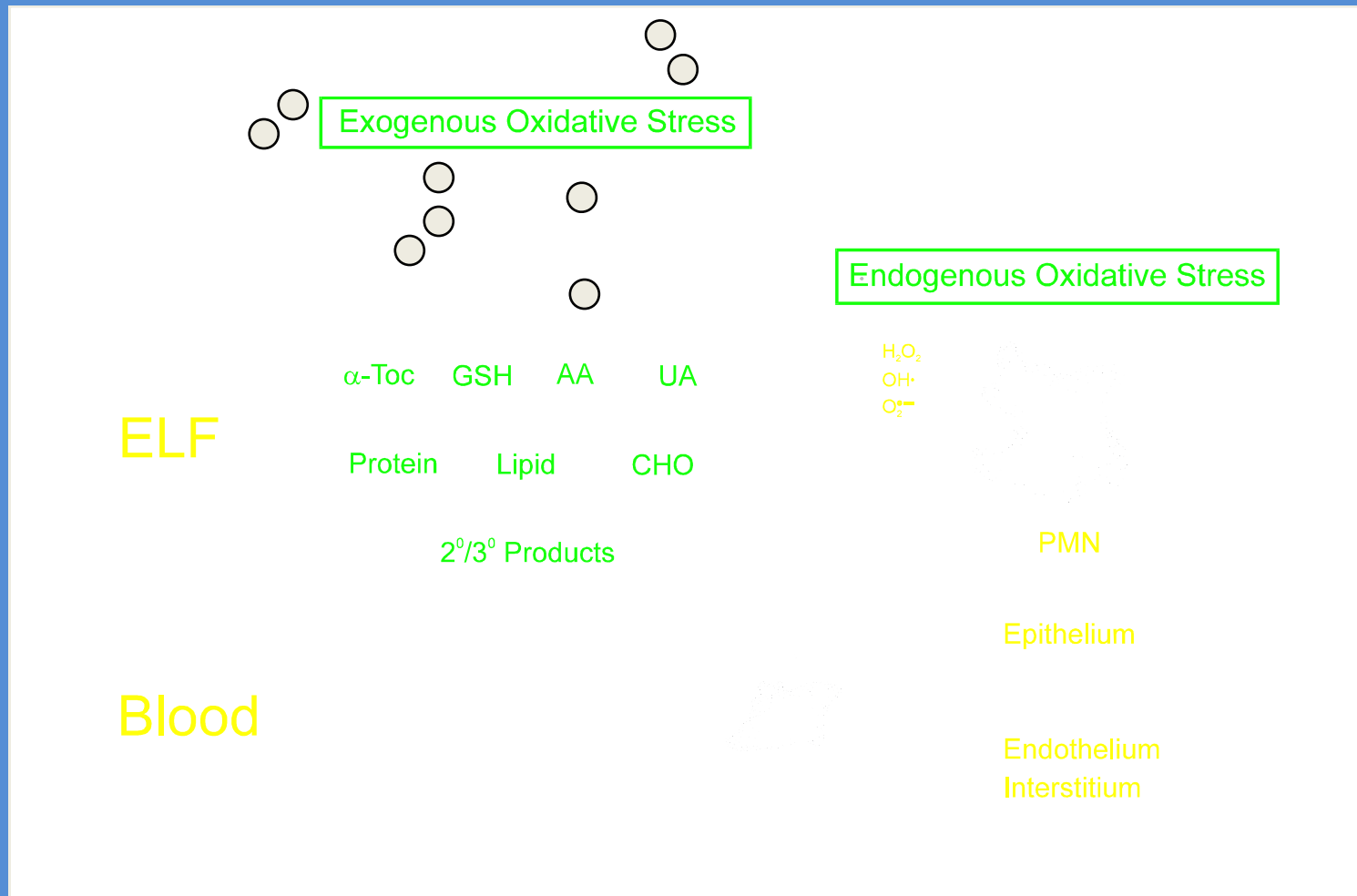
# Bronchoscopy

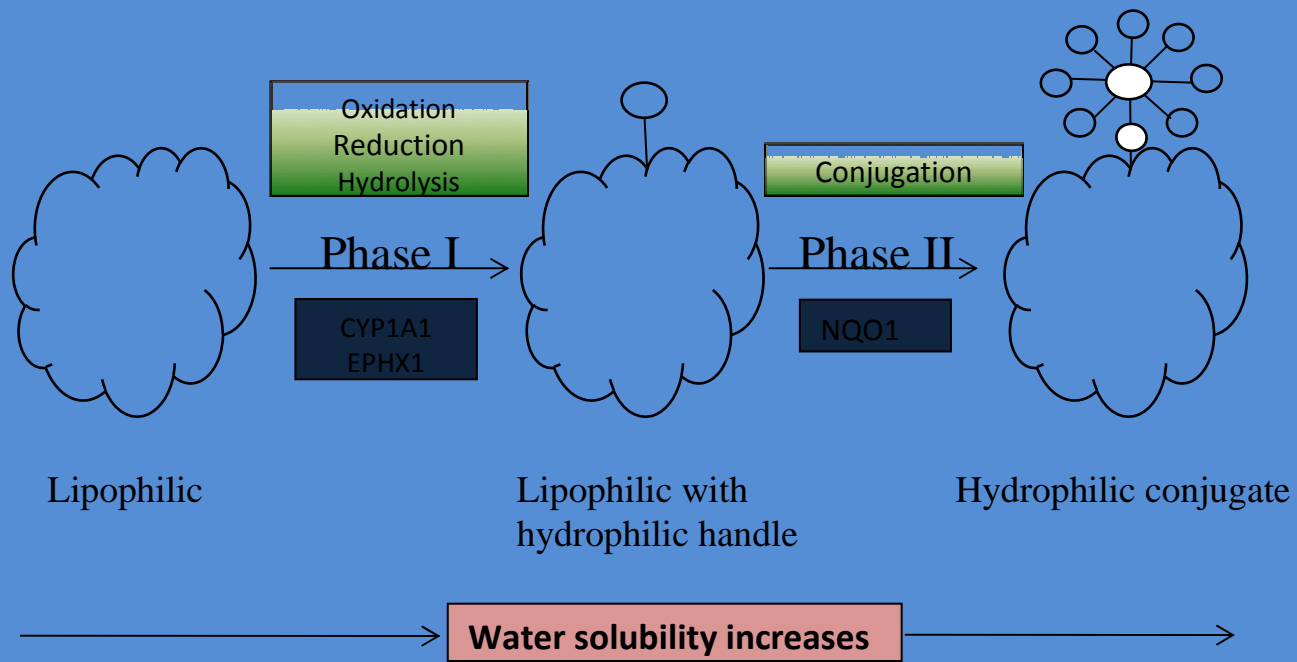


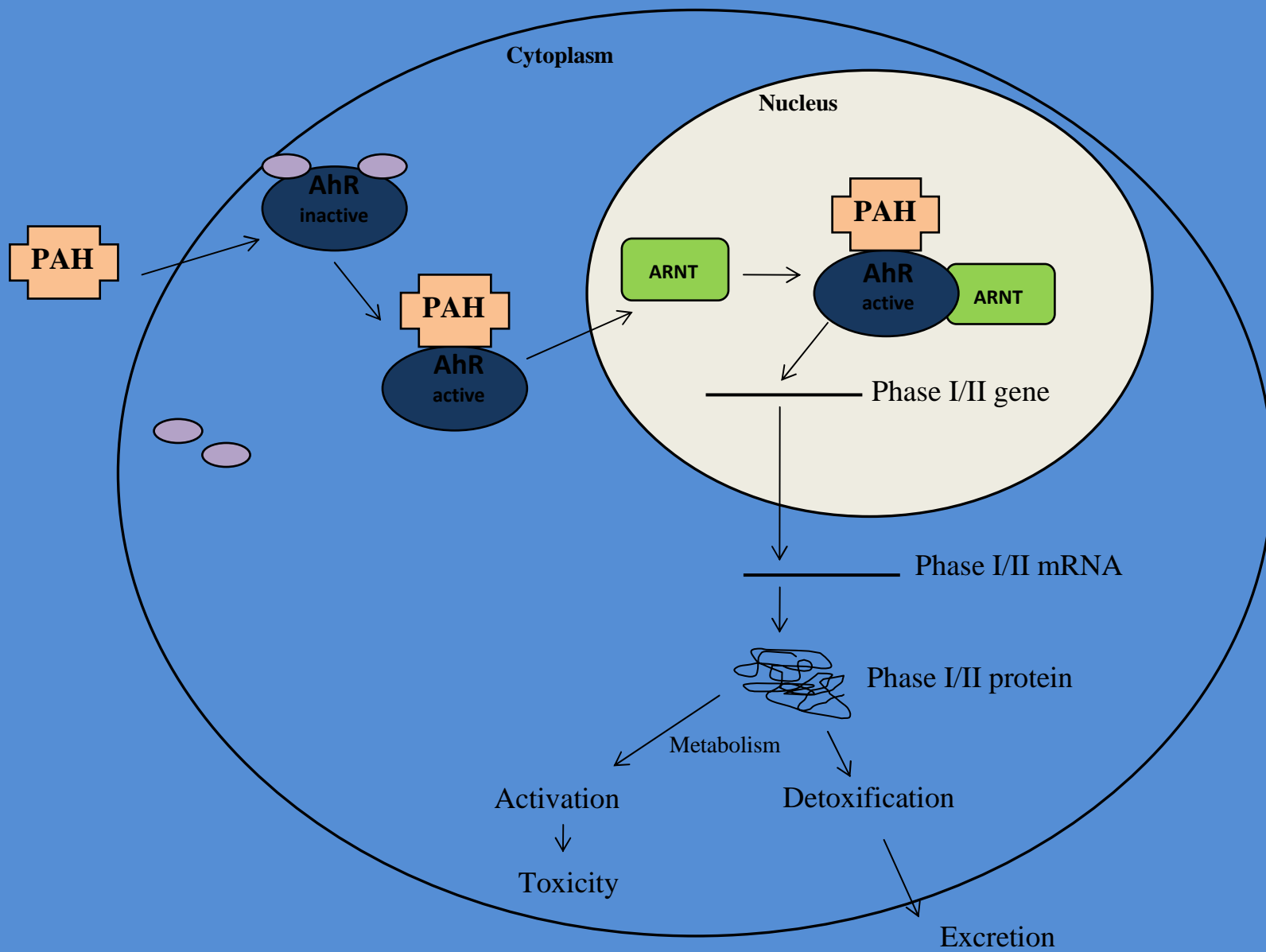
- Biopsies of airway wall tissue
- Bronchial wash (BW)
- Bronchoalveolar lavage (BAL)



# Oxidative stress of air pollutants

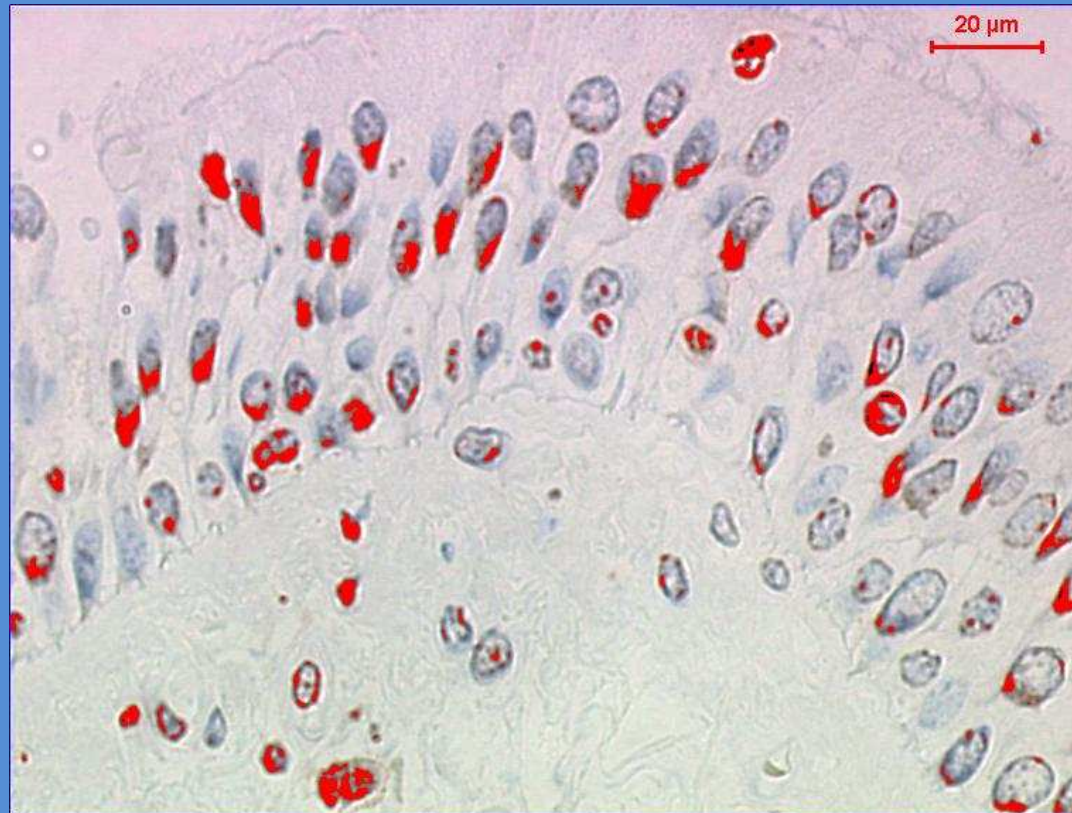






# Airway epithelial activation after primary oxidative reaction in respiratory tract lining fluid

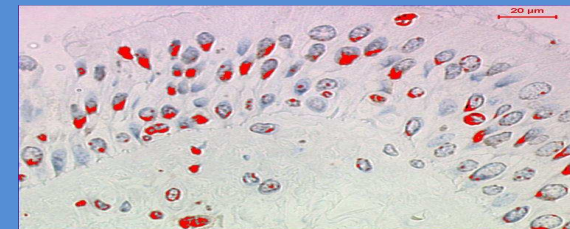
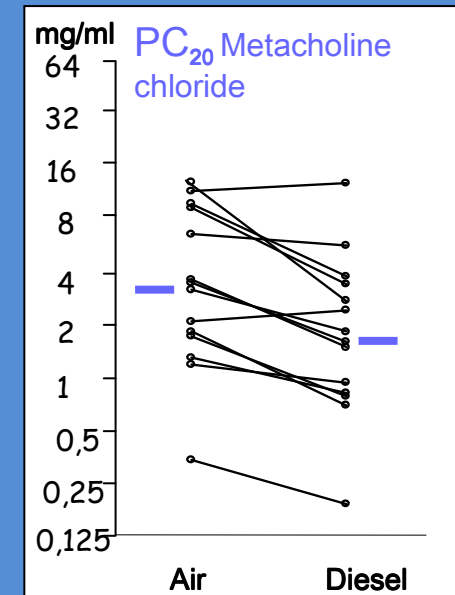
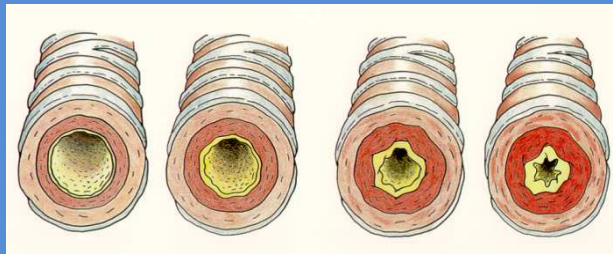
- NFkB
- AP-1
- P-38 MAPK
- JNK
- EGFR
- TLR



Pourazar et al. Am J Physio I-Lung Cell Mol Physiol 2005

Pourazar et al. Particle Fibre Toxicol, in press

# Worsening of asthma by diesel exhaust despite inhaled steroid medication



Nordenhall et al ERJ 2001

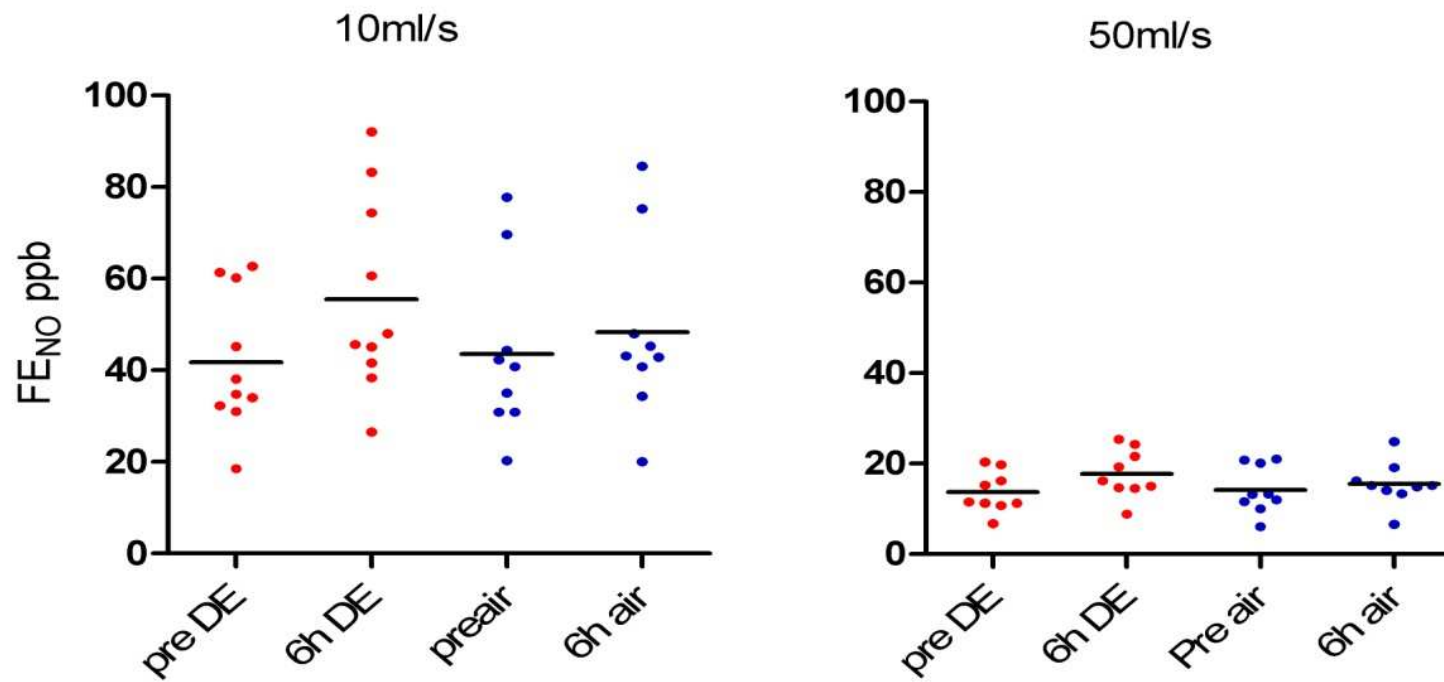
Stenfors et al ERJ 2004

Behndig et al Thorax 2010

# FENO



# Results



# Cardiovascular effects of Air pollution particles

*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

OCTOBER 21, 2004

VOL. 351 NO. 17

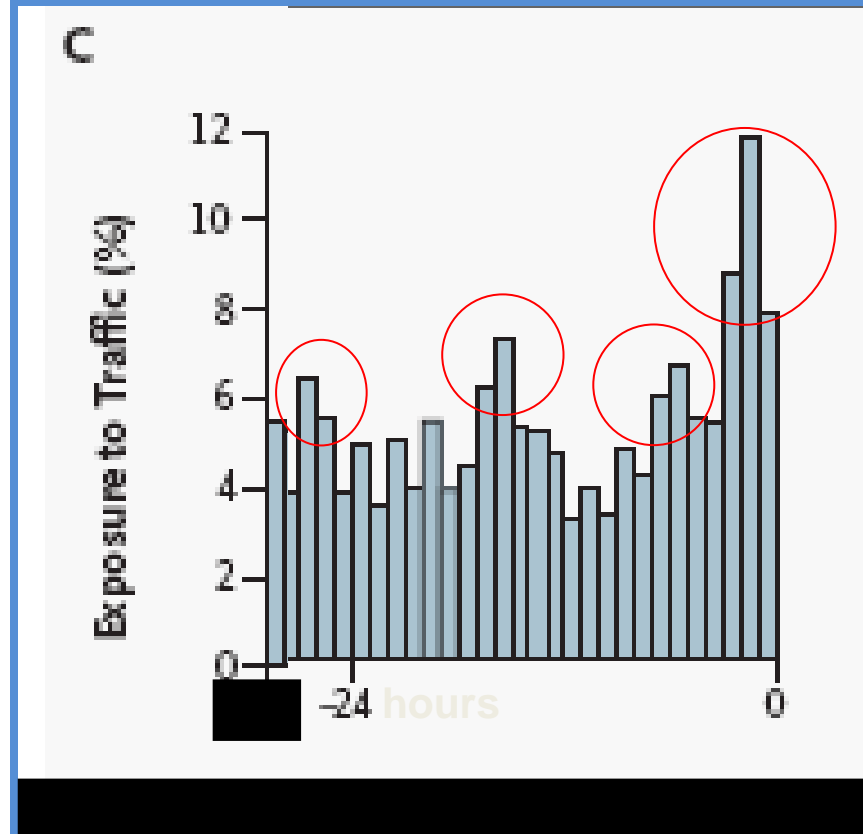
Exposure to Traffic and the Onset of Myocardial Infarction

Annette Peters, Ph.D., Stephanie von Klot, M.P.H., Margit Heier, M.D.,  
Ines Trentinaglia, B.S., Allmut Hörmann, M.S., H. Erich Wichmann, M.D., Ph.D., and Hannelore Löwel, M.D.,  
for the Cooperative Health Research in the Region of Augsburg Study Group

# Myocardial infarction in relationship to preceding traffic exposure

**Table 2.** Odds Ratios for the Onset of Myocardial Infarction (MI) after Time Spent in Traffic, According to the Means of Transportation.\*

Type of Transportation and Hours before MI	No. of Subjects	Frequency of Exposure in Case Period on Day of MI (%)	Odds Ratio (95% CI)	P Value
<b>Any means of transportation†</b>				
Concurrent	585	8.0	1.50 (1.07–2.09)	0.02
1 hr	625	12.1	2.92 (2.22–3.83)	<0.001
2 hr	634	8.9	2.01 (1.49–2.72)	<0.001
3 hr	635	5.5	1.15 (0.79–1.66)	0.47
4 hr	638	5.6	1.27 (0.89–1.83)	0.19
5 hr	639	6.8	1.64 (1.17–2.30)	0.004
6 hr	640	6.1	1.34 (0.93–1.92)	0.11
<b>Cars</b>				
Concurrent	585	5.6	1.33 (0.90–1.99)	0.15
1 hr	625	8.3	2.60 (1.89–3.57)	<0.001
2 hr	634	6.5	1.94 (1.37–2.76)	<0.001
3 hr	635	4.2	1.16 (0.76–1.78)	0.49
4 hr	638	4.0	1.21 (0.79–1.86)	0.38
5 hr	639	5.3	1.73 (1.19–2.54)	0.005
6 hr	640	5.0	1.55 (1.04–2.30)	0.03
<b>Bicycles</b>				
Concurrent	585	1.8	2.59 (1.27–5.29)	0.009
1 hr	625	2.4	3.94 (2.14–7.24)	<0.001
2 hr	634	1.6	2.70 (1.37–5.33)	0.004
3 hr	635	1.0	1.66 (0.74–3.74)	0.22
4 hr	638	0.7	1.16 (0.45–2.96)	0.76
5 hr	639	0.9	1.49 (0.63–3.54)	0.37
6 hr	640	0.7	1.02 (0.36–2.87)	0.97
<b>Public transportation</b>				
Concurrent	585	0.5	1.08 (0.33–3.55)	0.90
1 hr	625	1.2	3.09 (1.41–6.75)	0.005
2 hr	634	0.9	2.13 (0.91–5.23)	0.08
3 hr	635	0.3	0.69 (0.17–2.88)	0.62
4 hr	638	0.9	2.27 (0.95–5.41)	0.06
5 hr	639	0.6	1.54 (0.55–4.37)	0.41
6 hr	640	0.3	0.73 (0.17–3.06)	0.67



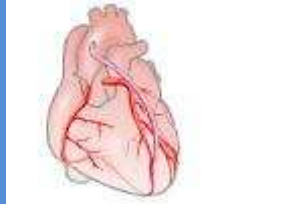
# Exposure to traffic is related to myocardial infarctions in Germany

- Inside car or bus
- Cycling
- Road side

Peak excess myocardial infarctions at

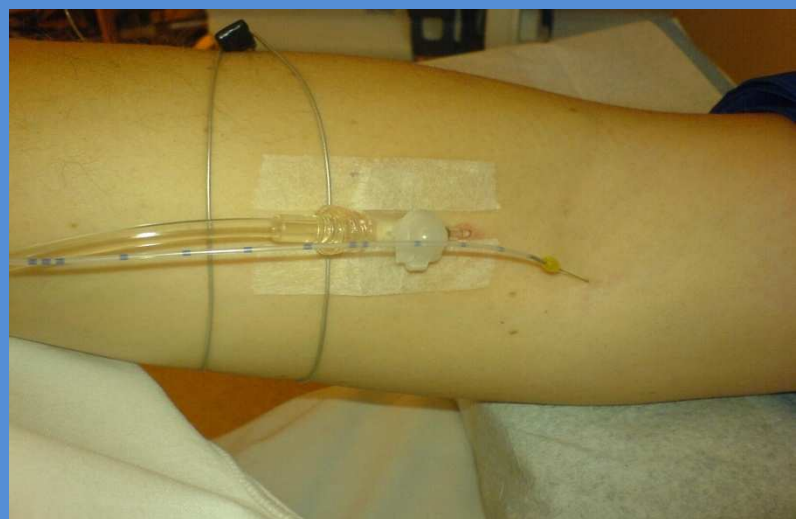
1-2 hours + 6-8 hours

# Particle effects potentially related to cardio-vascular events

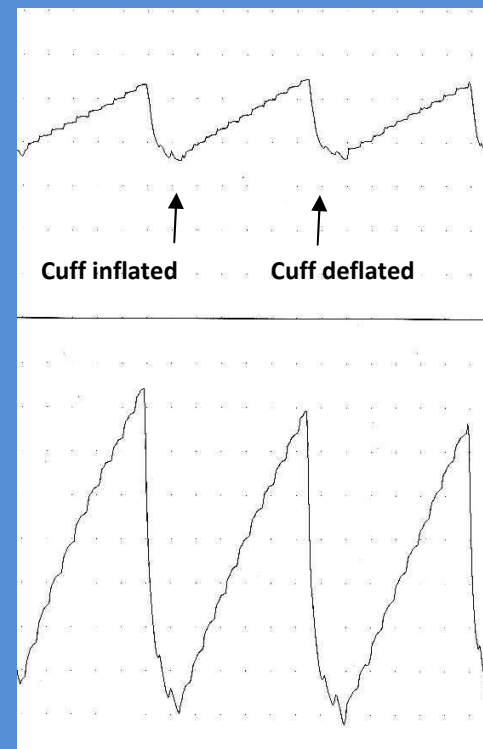


- Inflammation in the lungs
- Endothelial effects
- Smooth muscle dysfunction
- Activation of white blood cells and platelets
- Plasma viscosity
- Coagulation factors
- Plasminogen activator
- Plaque rupture
- Nitric oxide production
- Inflammatory components in the blood, fibrinogen, fibronectin, CRP, IL-6, IL-8, adhesion molecules, CD40L
- Local inflammation in the blood vessels and myocardium
- Congestive heart failure Heart rate variability
- Arrhythmias
- Depolarisation disturbance

# Venous Occlusion Plethysmography

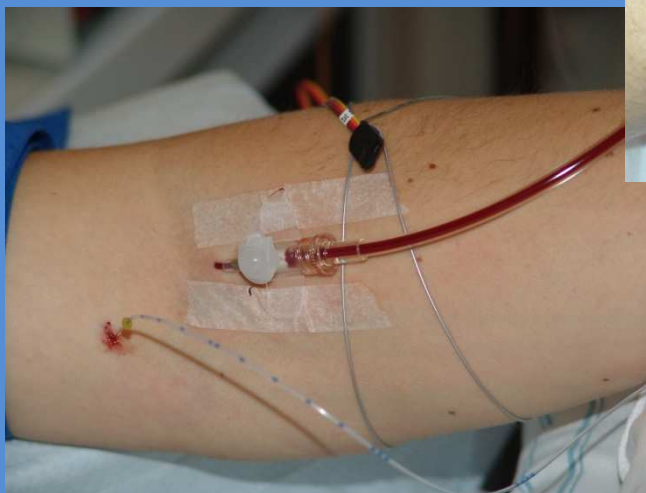


Non-infused arm



Infused arm

# Venous occlusion forearm plethysmography

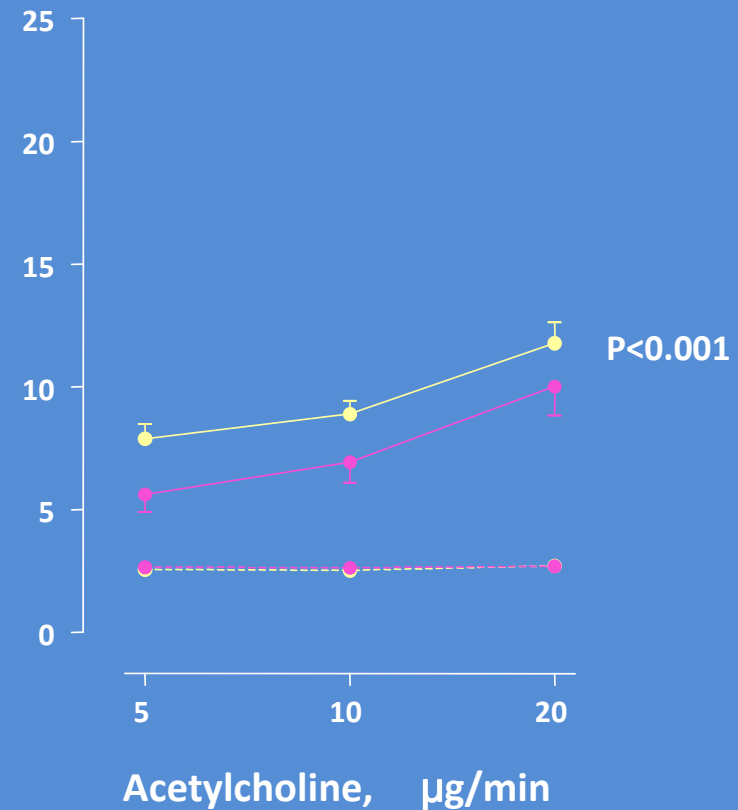
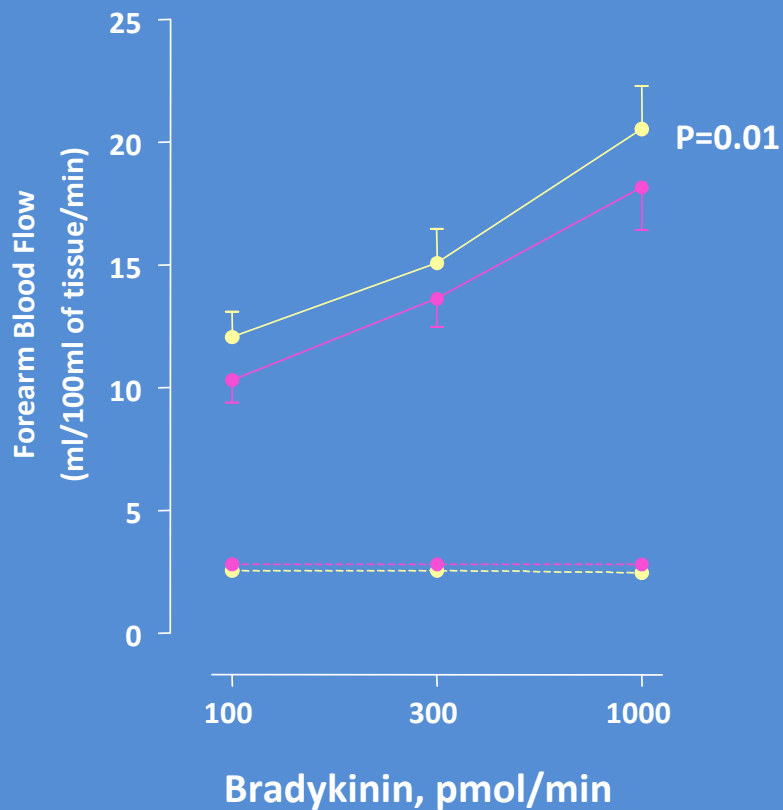


## The Drugs



# Endothelium-Dependent Vasodilatation

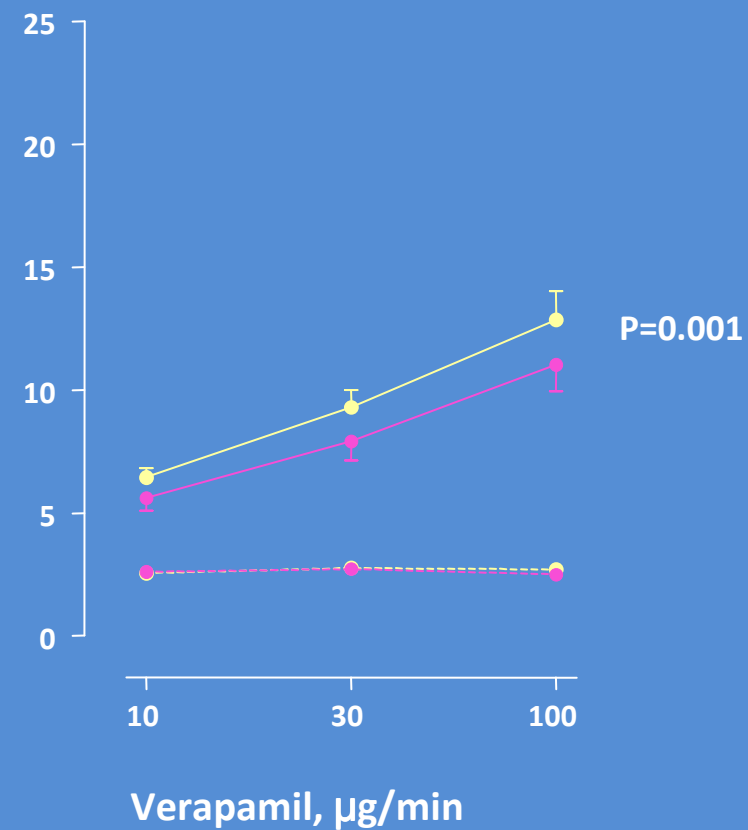
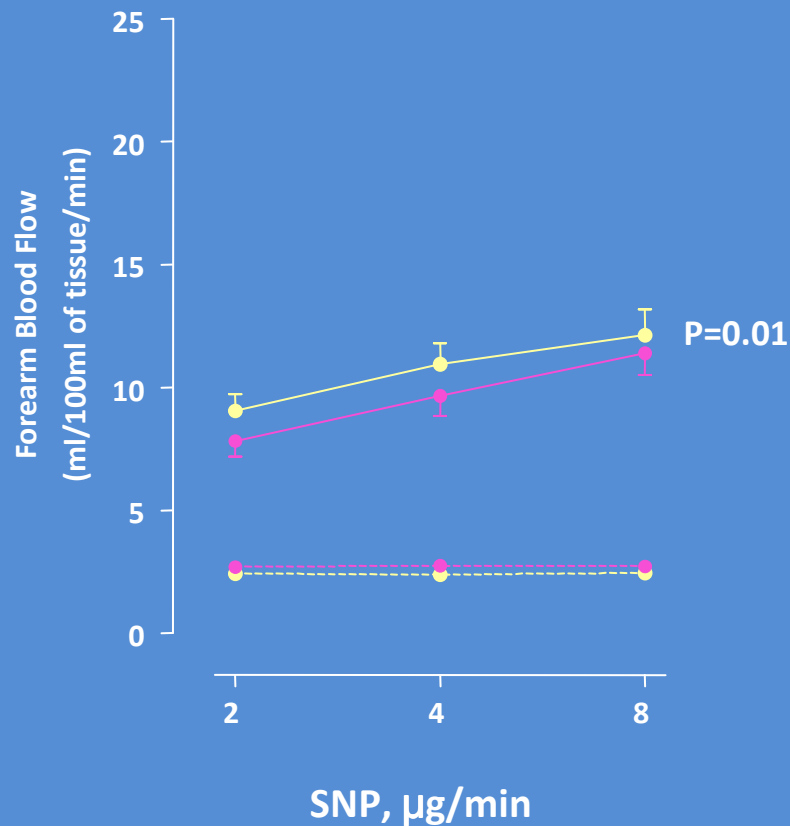
FILTERED AIR *versus* DIESEL EXHAUST



Infused (solid line) and non-infused (dashed line) forearm blood flow following diesel (●) and air (●) during intra-brachial infusion of bradykinin and acetylcholine.

# Endothelium-Independent Vasodilatation

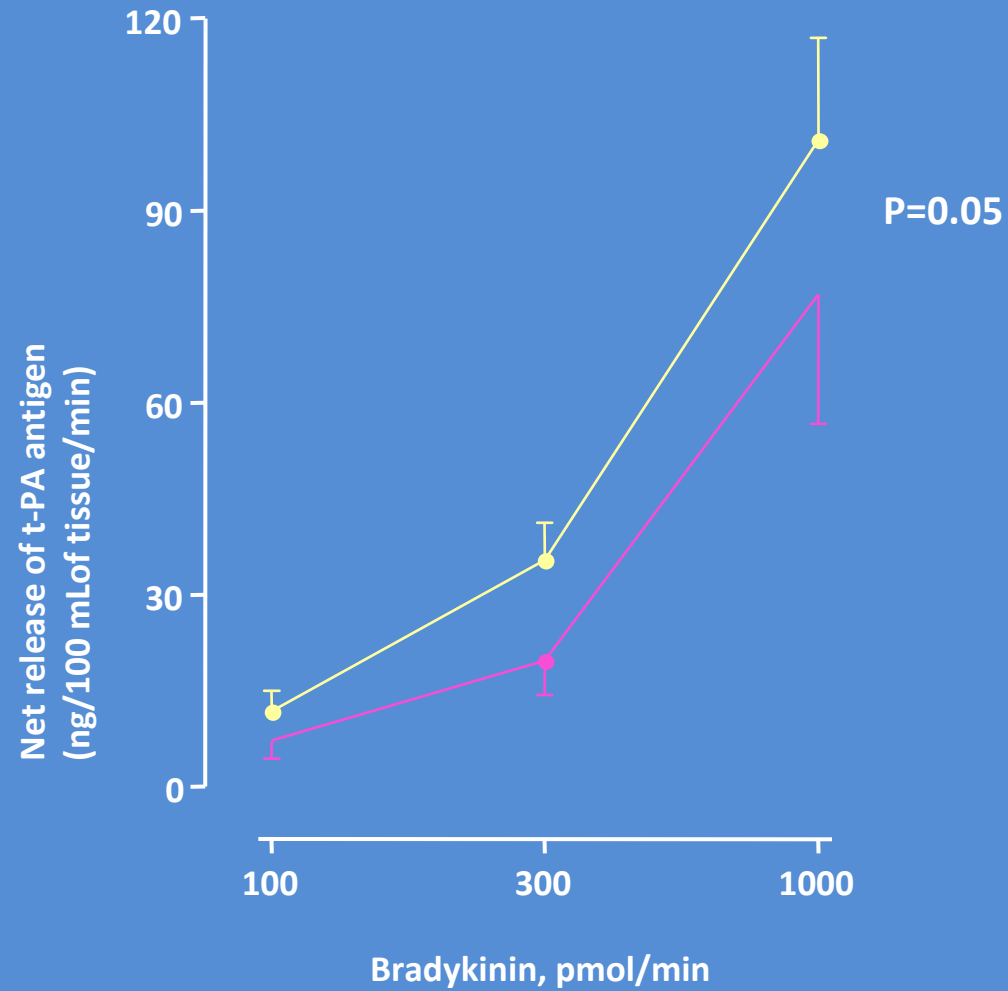
FILTERED AIR *versus* DIESEL EXHAUST



Infused (solid line) and non-infused (dashed line) forearm blood flow following diesel (●) and air (●) during intra-brachial infusion of sodium nitroprusside and verapamil.

# Endogenous Fibrinolysis

FILTERED AIR *versus* DIESEL EXHAUST



# Arterial Stiffness

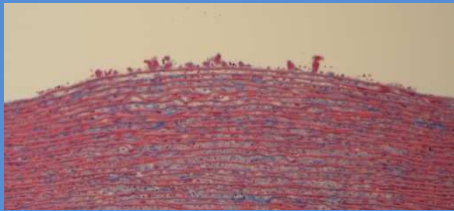
- A non-invasive means of addressing vascular function – endothelial function
- Peripheral Pulse Wave – Transfer function – Central Pulse Wave



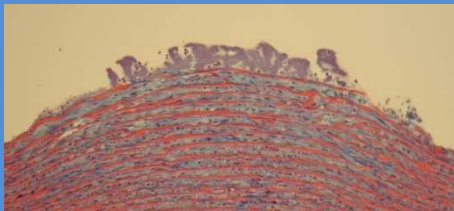
# Thrombosis formation ex-vivo



Air

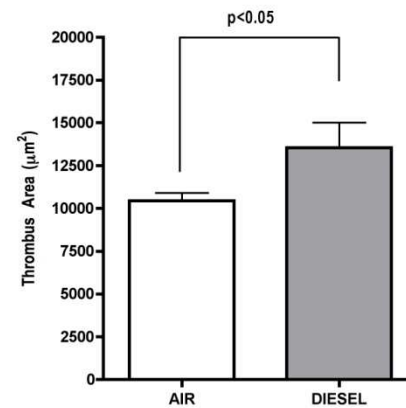


Diesel

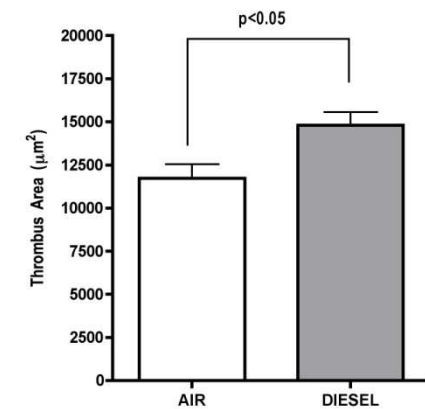


Low Shear Chamber

2 HOURS

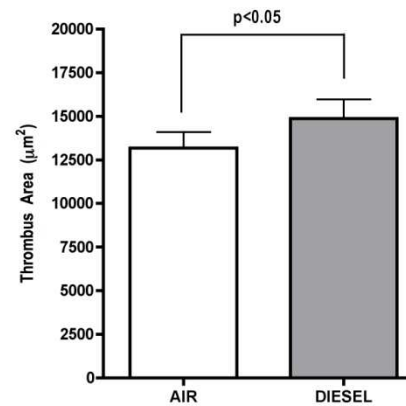


6 HOURS

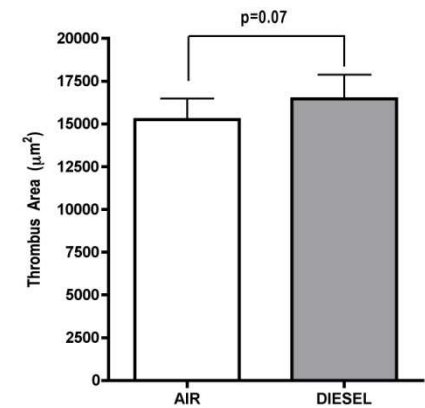


High Shear Chamber

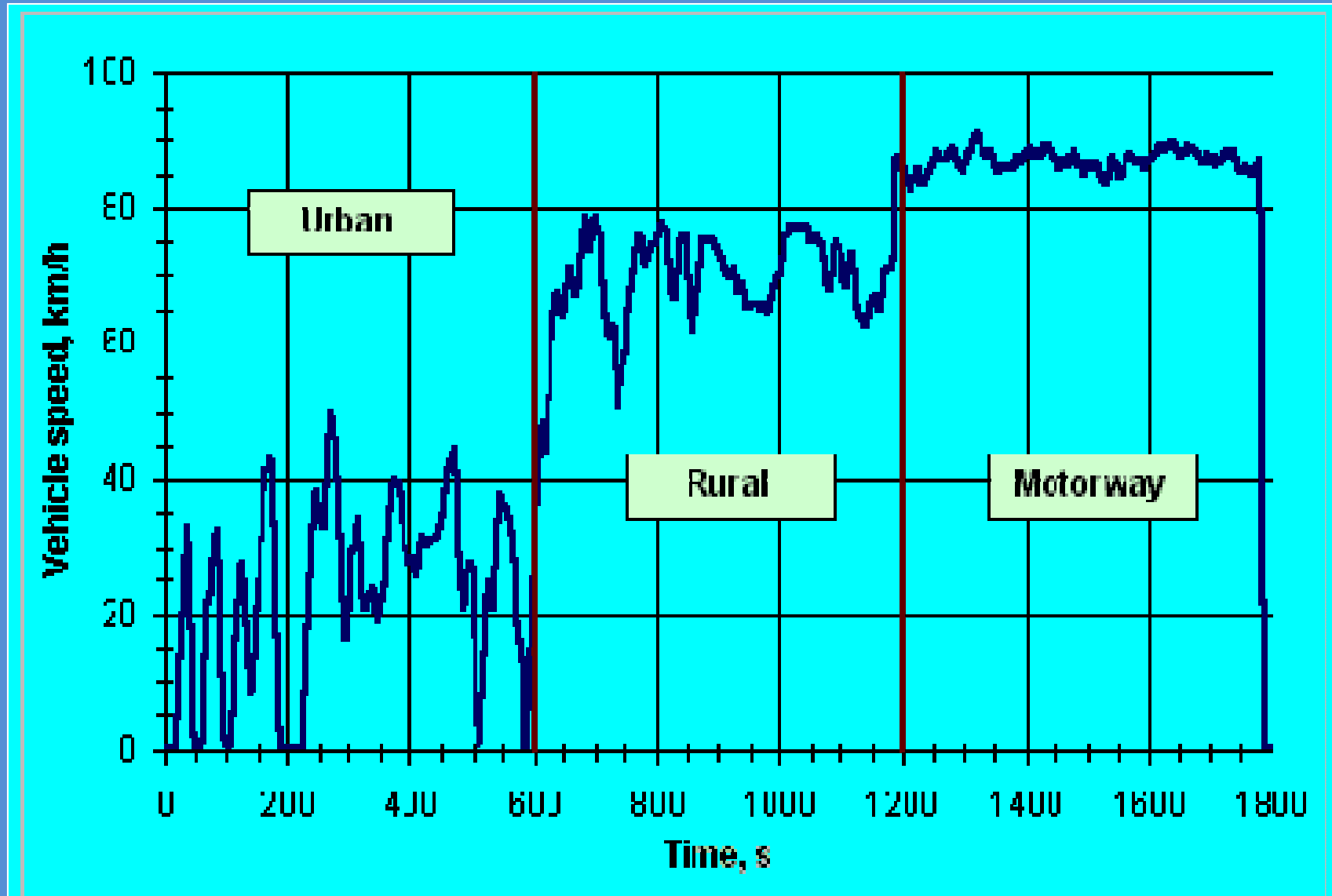
2 HOURS



6 HOURS



# European Transient Cycle (ETC)



# Chamber Concentrations Idling Versus ETC

	Idling	ETC, Urban
NO (ppm)	2.2±<0.1	6.6±0.3
NO <sub>2</sub> (ppm)	0.6±<0.1	0.9±0.2
No <sub>x</sub> (ppm)	2.8±0.1	7.5±0.3
Total HC (ppm)	1.6±0.2	1.2±0.2
Mass (μg/m <sup>3</sup> )	330±12	254±38
Organic carbon fraction (OC/TC), %	94.5	12
Elemental carbon fraction (EC/TC), %	5.5	88
Total PAH concentration (μg/m <sup>3</sup> )	3.5	0.96
Particle number concentration, #/cm <sup>3</sup>	9.5×10 <sup>5</sup>	1.2×10 <sup>5</sup>

# DIESEL and vascular effects

- Diesel exhaust from idling – more hydrocarbons
- Diesel from European Transient Cycle – urban part
- Diesel from engine in Edinburgh
- Consistent effects for over 24 hours
- Filtering of PM and keeping the gases diminished the effects

# Diesel exhaust mechanisms

- L-NMMA
- SNP
- Decreased nitrate levels
- Decreased NO availability
- Consistent with oxidative stress

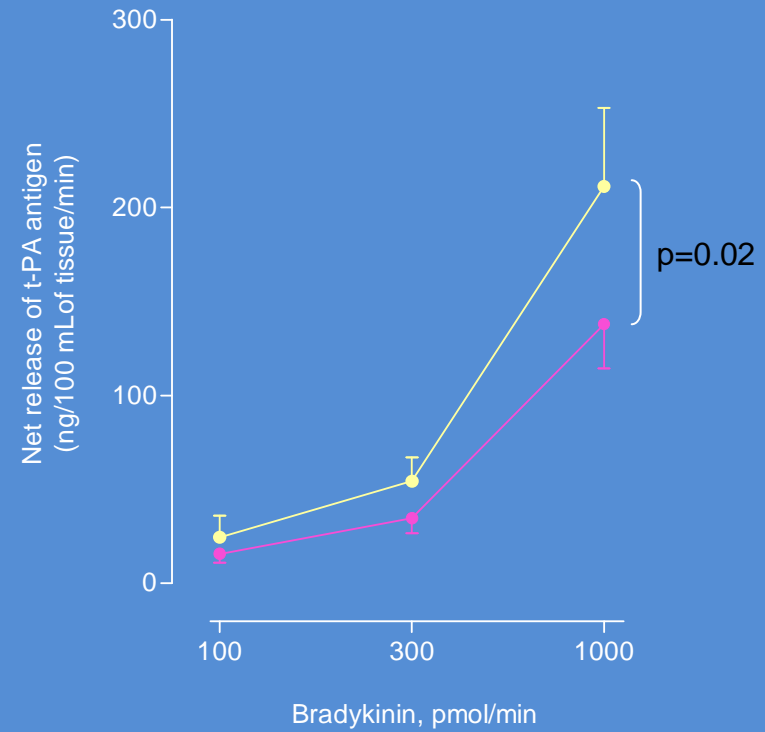
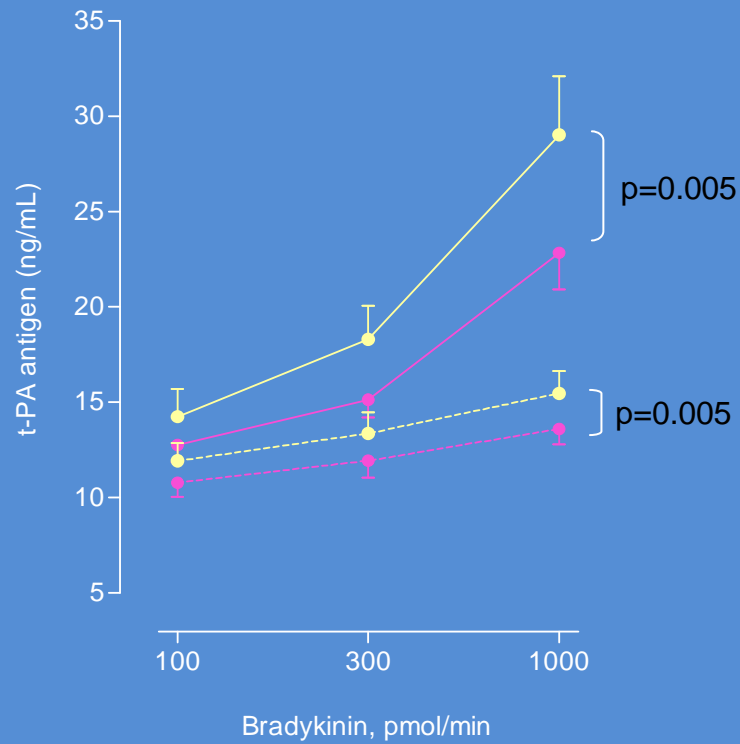
# Diesel exhaust effects in Heart patients

- 20 male subjects
- Coronary Stenosis treated by PCI
- Normal exercise test
- No symptoms
- Totally stable
  
- Proven coronary and vascular disease but not at risk at present time
- On full preventive medication
  
- No diabetes or tendency for congestive heart failure

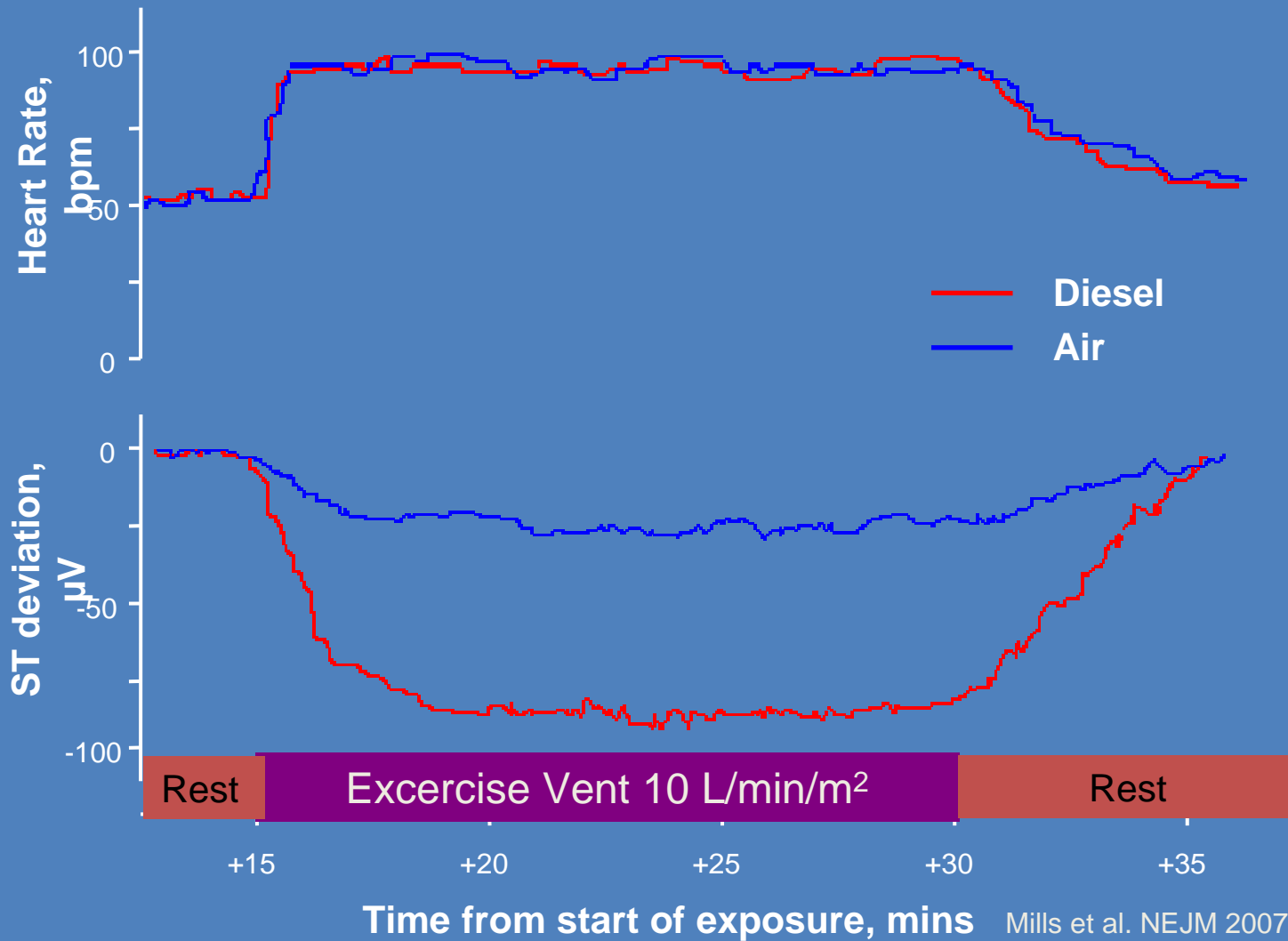
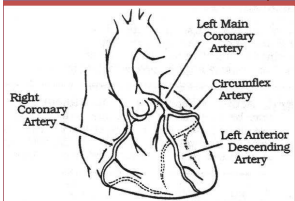
## Diesel exhaust effects in Heart patients

- Stiff blood vessels not responsive for further vasodilation
- Endothelial function and anti-thrombotic functions critical
- Especially at risk at plaque rupture

# Diesel exposure impairs endogenous fibrinolysis in subjects with ischemic heart disease



# Exercise induced ischaemia reflected by 12-lead HOLTHER ECG



# Antioxidant defences

# Oxidative Stress

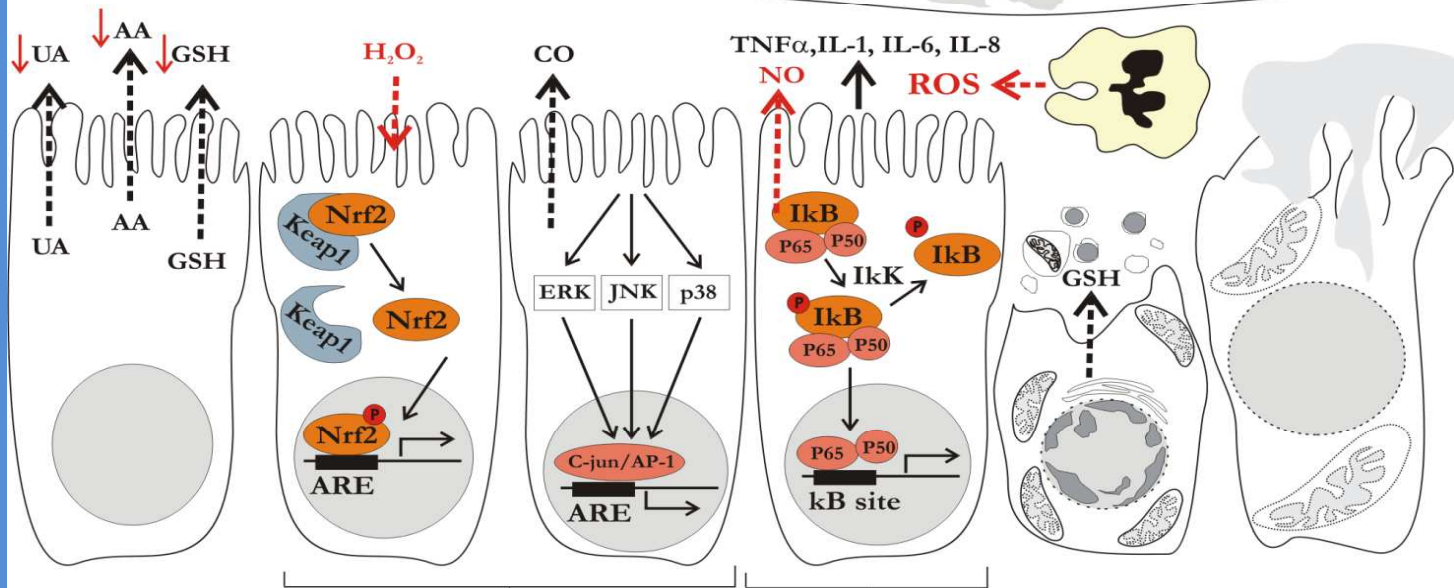
↓ GSH/GSSG<sub>cell</sub>

Protection

Adaption

Inflammation

Cell death



- GST
- NQO1
- GCLc/m
- GGT
- UGT
- Trx reductase
- Trx peroxidase
- heme oxidase-1
- ferritin

- Cytokines
- Chemokine
- iNOS
- COX
- Antimicrobial peptides
- IκB
- Anti apoptotic proteins
- Cyclin D1, c-MYC

Apoptosis Necrosis

Support for Diesel exhaust to mechanistically  
link to respiratory and  
cardiovascular health effects

- Heart and vascular effects in healthy and heart patients, despite extensive treatments
- Increased hyperresponsiveness in asthmatics, despite inhaled steroids
- Airway inflammatory patterns