

## Traffic Related Pollution: Risk Factor for the Development of Cardiovascular Diseases?

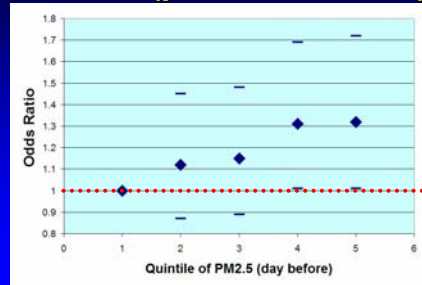


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Prepared for the 11<sup>th</sup> ETH Conference on Combustion Generated Nanoparticles, Zurich, August 14<sup>th</sup>, 2007 – Session 8:30-10:00



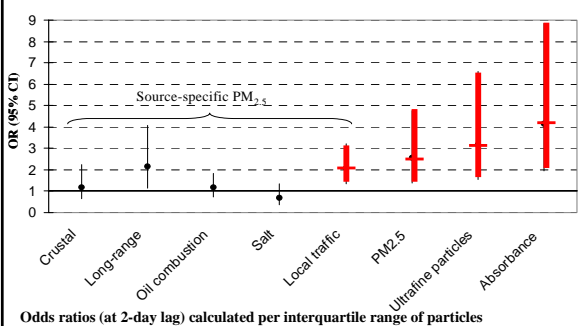
## Myocardial Infarction is associated with PM<sub>2.5</sub> (previous 24 hrs.)



Peters A. et al. Circulation 2001

## Exercise induced ST segment depressions (Indicator of Ischemia)

Lanki T, Environ Health Perspect, 2006



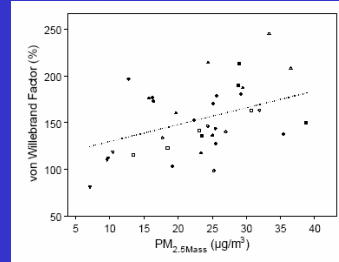
Odds ratios (at 2-day lag) calculated per interquartile range of particles

## Association of cardiovascular measures with ambient PM among 9 healthy highway patrol troopers (4 shifts each)

Riediker et al., AJRCCM 2004

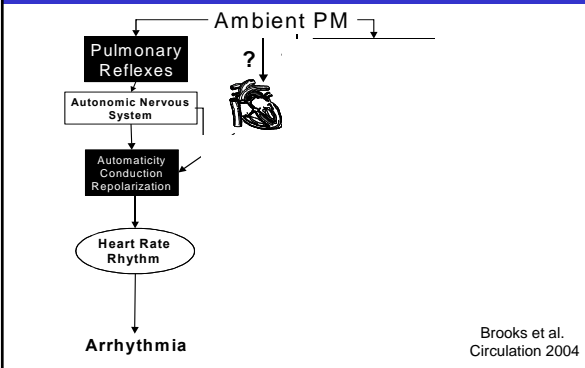
Significant associations of in-car PM with:

- Lymphocytes ↓
- Increased:
  - mean corpuscular volume,
  - Neutrophils,
  - CRP,
  - von Willebrand factor,
  - Heart beat cycle length (next morning),
  - Ectopic beats,
  - Changes in HRV



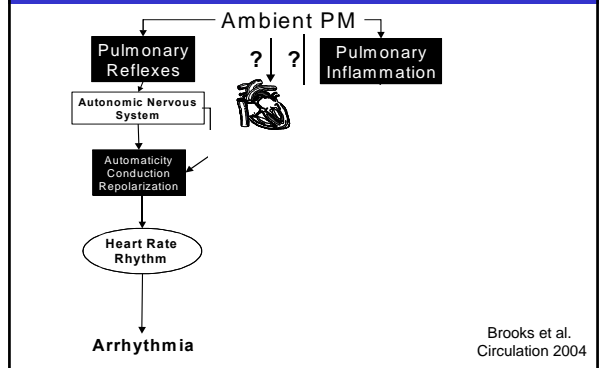
E1C

## Acute Cardiovascular Effects of Ambient Air Pollutants

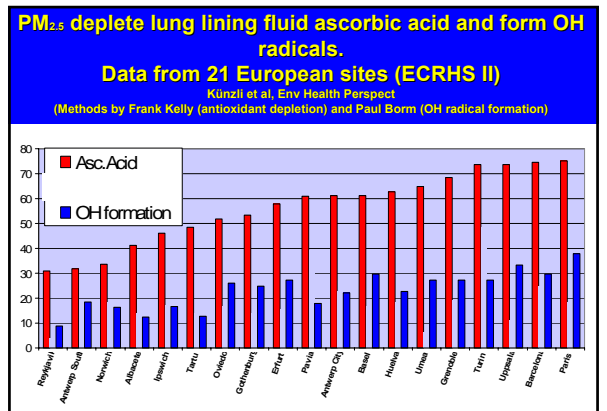
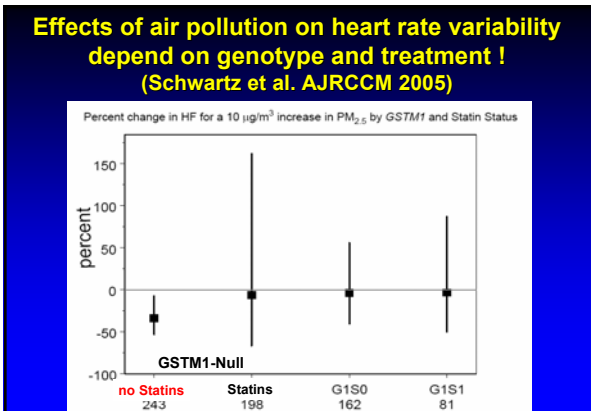
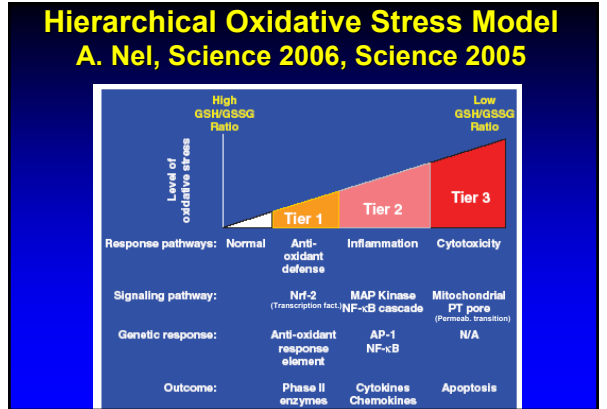
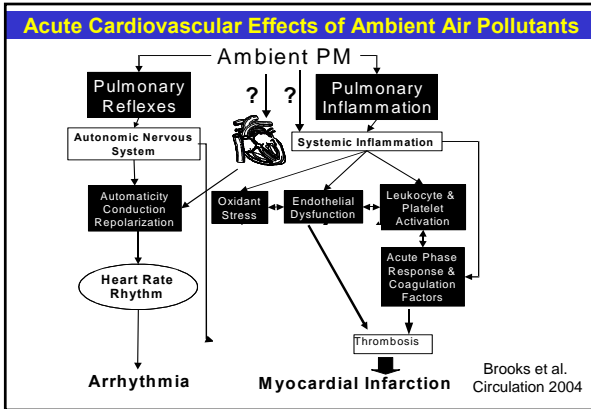


Brooks et al. Circulation 2004

## Acute Cardiovascular Effects of Ambient Air Pollutants



Brooks et al. Circulation 2004

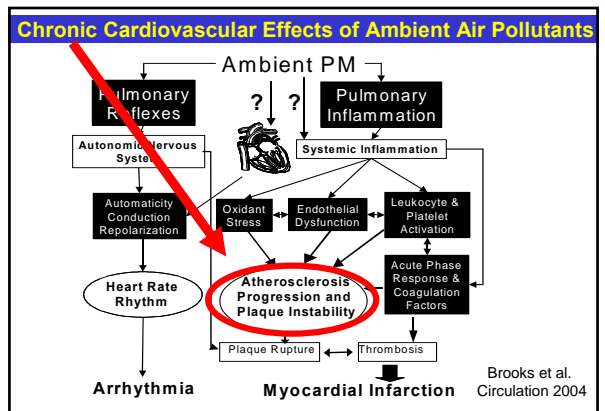
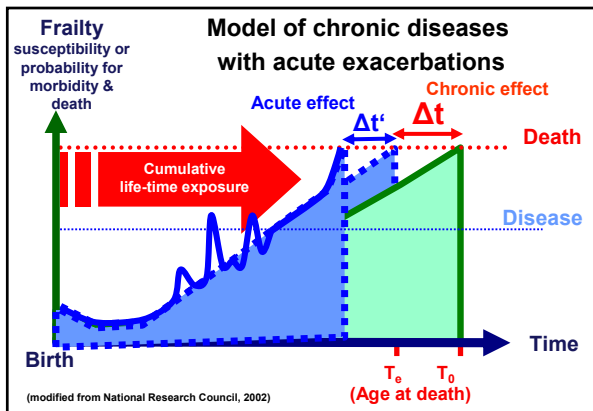


- ### Most investigated acute cardiovascular effects of air pollution
- Increase in daily death rates
  - Myocardial infarction
  - Stroke
  - Arrhythmia
  - Change in coagulation factors

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### Atherosclerosis

Lusis, Nature 2000

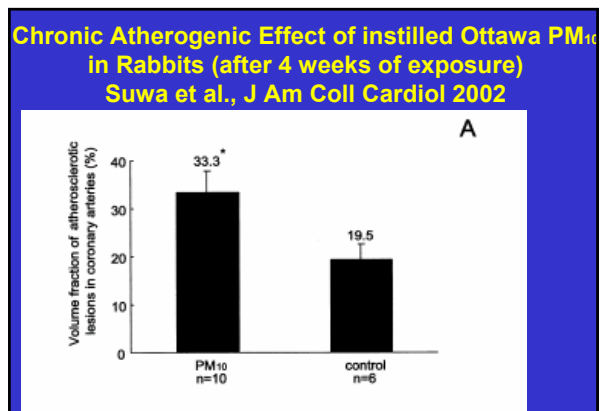
1. Endothelial dysfunction & retention of lipids
2. Lipid accumulation and oxidation in intima
3. Monocyte & lymphocyte recruitment (inflammation)
4. Proliferation of macrophages
5. Foam cell formation
6. Fibrous plaque formation
7. Extracellular degradation
8. Rupture / Thrombosis (ACUTE EVENTS)

### Is air pollution atherogenic ?

### Effect of instilled Ottawa PM<sub>10</sub> in Rabbits (after 4 weeks of exposure)

Suwa et al., J Am Coll Cardiol 2002;  
Goto et al. AJRCCM 2004;  
Goto et al. Am J Phys Lung Cell Mol Phys 2004;

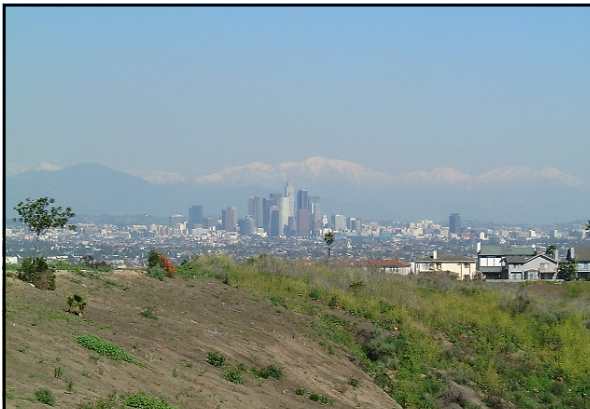
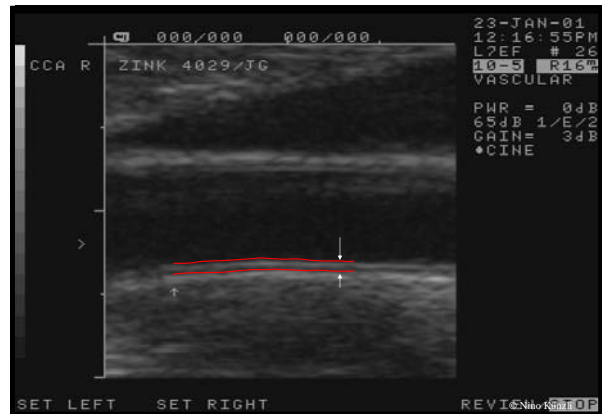
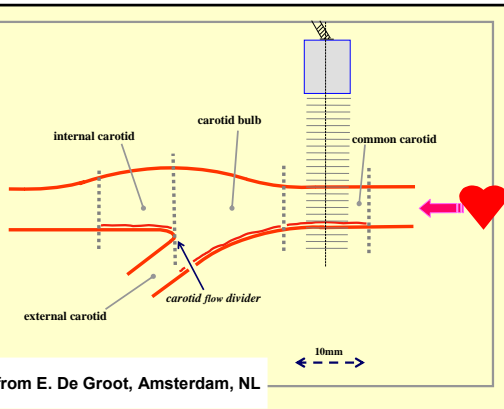
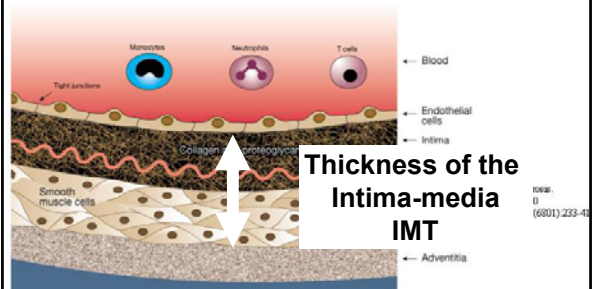
- Increase in circulating polymorpho-nuclear leucocytes
- Stimulation of bone marrow release of monocytes
- Increase in macrophages containing PM10
- Higher atherosclerosis lesion scores (in coronary artery and aorta)
- More advanced lesions
- Lesions correlated with amount of PM10 uptake in alveolar macrophages



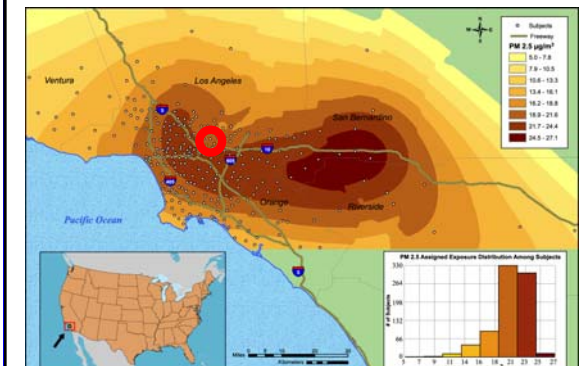
Is air pollution atherogenic... in humans ?

## Measuring Atherosclerosis

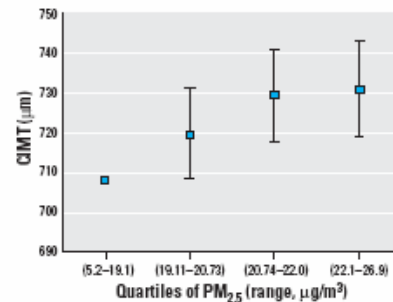
Structure of a normal large artery



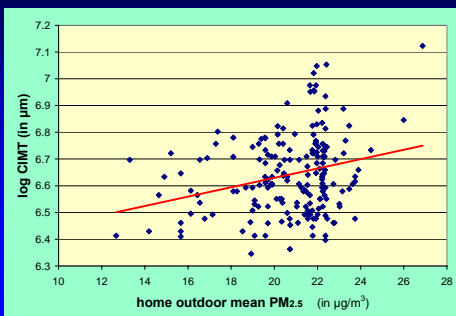
## EXPOSURE SURFACE, PM<sub>2.5</sub>



## Home outdoor PM<sub>2.5</sub> is associated with CIMT Künzli et al, Env Health Perspect 2005



## Association between artery wall thickness (CIMT) and home outdoor mean PM<sub>2.5</sub> in women, age 60 and older (from Künzli et al., Air Pollution and Cardiovascular Disease; Harrison Online 2005)



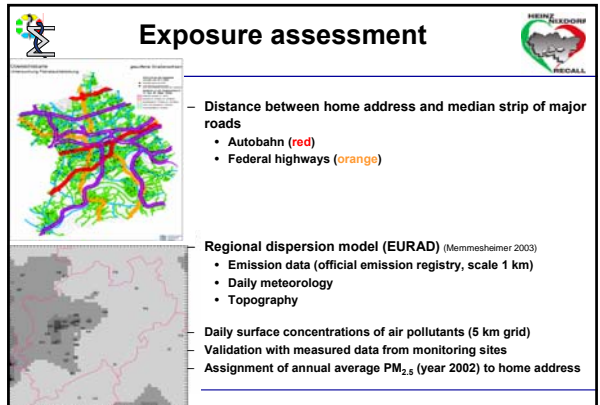
## ONGOING IMT-STUDIES

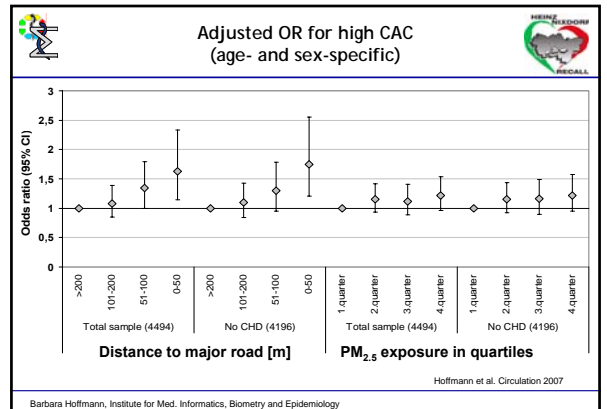
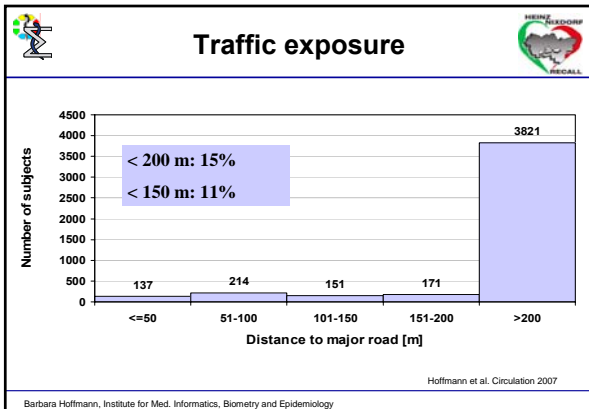
- in children: USC Children's Health Study (NIEHS)
- in adolescents (USC College students) (NIEHS)
- in population-based sample of adults (Spanish REGICOR study, Girona) (Spanish Ministry FIS-Grant); KORA Augsburg (A. Peters)
- others.....

## Heinz Nixdorf Recall Study (Hoffmann et al, Circulation 2007)

- Random population sample from 3 areas (Essen, Muhlheim, Bochum)
- ~4'800 subjects 45-73 yrs of age
- Baseline: 2000-2003
- Main outcome of pre-clinical state of atherosclerosis: Coronary artery calcifications (CT-scans)

## Exposure assessment





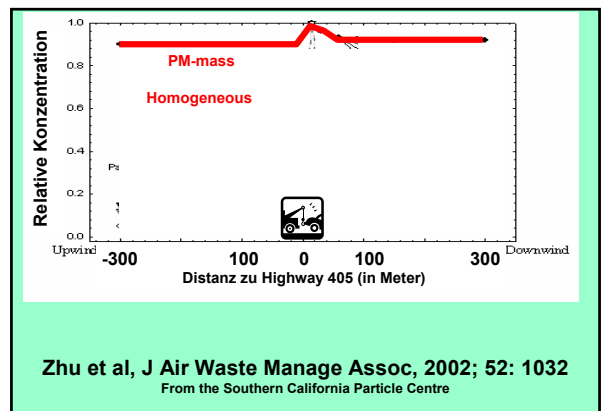
### Increasing evidence

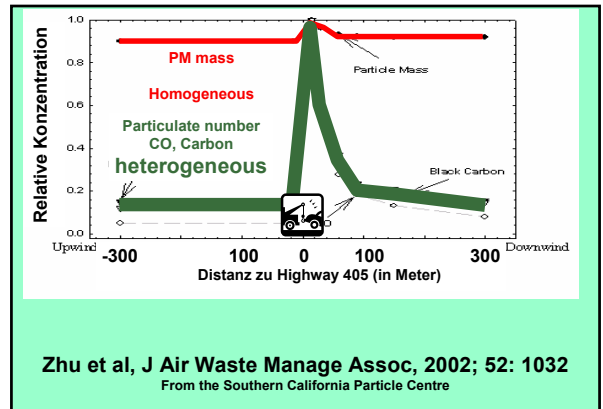
- Ambient air pollution triggers cardiovascular events...
- .... and may contribute to atherogenesis (strong experimental evidence!)

### BUT....

### Is it TRAFFIC-related pollution ?

- Primary emissions ?
- Secondary pollutants ?
- Re-suspension ?
- Contribution of coarse - fine - ultrafine - nano-PM ?
- Interaction of all the above ?





**Is it a NANO-PM effect?**

**Ratio of 'Highway' to 'Urban background' concentration of different PM size fractions**  
Ntziachristos et al. Atmos Environ August 2007

Size fraction (nm)	ratio Hwy710/urban
100-180	2.10
56-100	2.48
32-56	1.49
18-32	0.94

**Mechanisms**

**Ultrafine Particles Cross Cellular Membranes by Nonphagocytic Mechanisms in Lungs and in Cultured Cells**  
Marianne Gieseler<sup>1</sup>, Barbara Rothemann-Rothhausen<sup>2</sup>, Nadine Kapp<sup>1</sup>, Samuel Schorch<sup>1,2</sup>, Wolfgang Kreyling<sup>2</sup>, Holger Schulz<sup>1</sup>, Manafra Semmler<sup>1</sup>, Vincenzo Im Hof<sup>4</sup>, Joachim Heyder<sup>1</sup>, and Peter Gehr<sup>1</sup>

**Toxic Potential of Materials at the Nanolevel**  
Andre Weil<sup>1,2</sup>, Tian Xia<sup>2</sup>, Lutz Mädler<sup>1</sup>, Ming Li<sup>2</sup>

**Upregulation of Cyclooxygenase-2 by Motorcycle Exhaust Particulate-Induced Reactive Oxygen Species Enhances Rat Vascular Smooth Muscle Cell Proliferation**  
Hsui-Ping Tzeng<sup>1,2</sup>, Rong Sen Yang<sup>2,3</sup>, Tzau-Huei Ueng<sup>3</sup>, and Shing-Hwa Liu<sup>4,5,6</sup>

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- NEEDS**
- Chronic effect studies
  - Integrated exposure assessment for sources and constituents
  - Measurement of biologically-relevant aspects of exposure
  - Assessment of exposure to PM of various size fractions, including the nano-PM scale



CREAL

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Centre for Research in Environmental Epidemiology, Barcelona

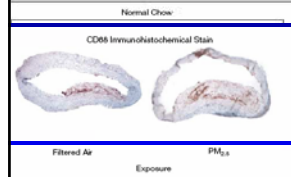
Gracias - Thank you

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## Atherosclerotic plaques after 6 months of exposure to New York PM in mice with normal and high fat chow

Sun et al, JAMA Dec 2005

Figure 2. Representative Photomicrographs of Hematoxylin-Eosin Staining and CD68 Immunohistochemical Staining of Abdominal Aortic Sections, and Oil Red-O Staining of Aortic Arch Sections



## Traffic-related pollution: Better knowns – ...

- Very high contribution to exposure to primary and secondary pollutants
- Many pollutants (mixture)
- Many effects (mechanisms) well described for several toxicants
- Traffic-related pollution IS a health problem

## Traffic-related pollution: ... – less knowns

- Contribution of specific pollutants to the orchestrated effects?
- Emissions versus re-suspension?
- Interactions between constituents?
- Health benefit of specific technological interventions / policies?
- Role of host factors (susceptibility)