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Insights from toxicology on health impacts of air pollution

Dr. Roel Schins

June 24th, 2020

Online EAERE pre-conference workshop

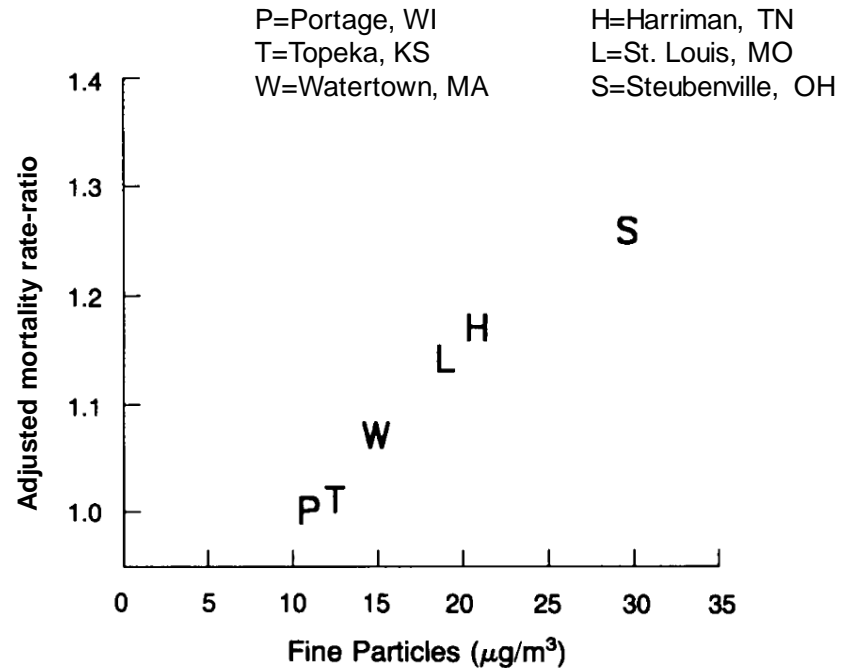
“The economic impacts of air pollution and the
implications for policy”

Mitglied der

Leibniz
Leibniz-Gemeinschaft

The Harvard Six Cities Study

Dockery *et al.* (1993). An Association between Air Pollution and Mortality in Six U.S. Cities, *NEJM* 329 (24):1753-1759.

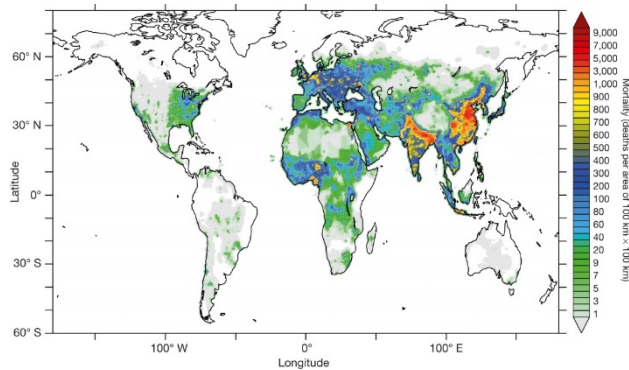


...“Although the effects of other, unmeasured risk factors cannot be excluded with certainty, these results **suggest that fine-particulate air pollution, or a more complex pollution mixture associated with fine particulate matter, contributes to excess mortality** in certain U.S. cities.”...

Toxicology of ambient particulate matter (PM)

World Health Organisation (WHO)

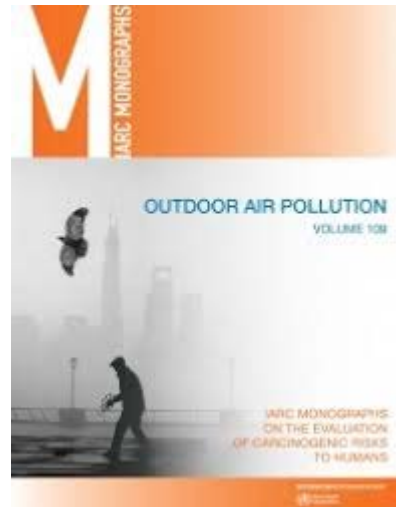
Ambient Air Quality Guidelines
“exceeded for > 90% of world’s population”



J Lelieveld *et al.* *Nature* **525**, 367-371
(2015) doi:10.1038/nature15371

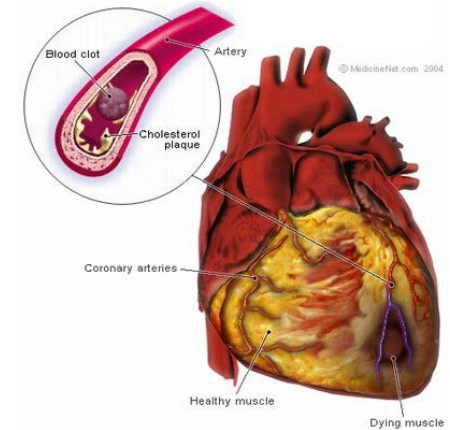
International Agency for Research on Cancer (IARC)

Outdoor air pollution and PM
classified as “carcinogenic to humans” (2013)

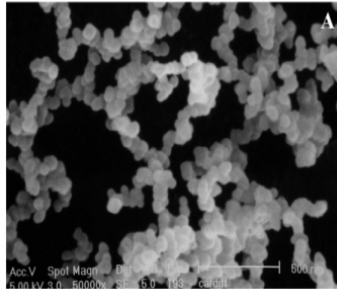


Ambient ultrafine particles

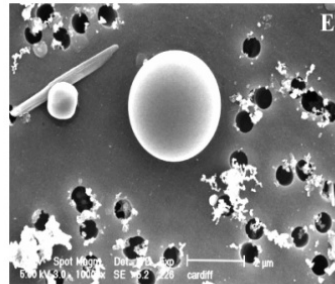
New target organs and emerging diseases



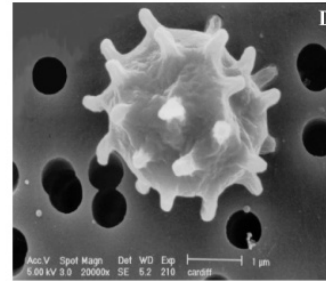
PM, a complex mixture....



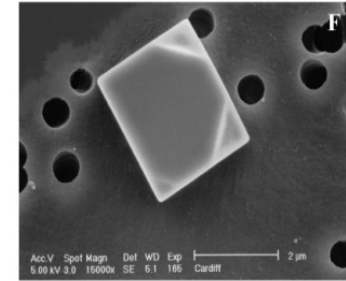
Soot



Metals



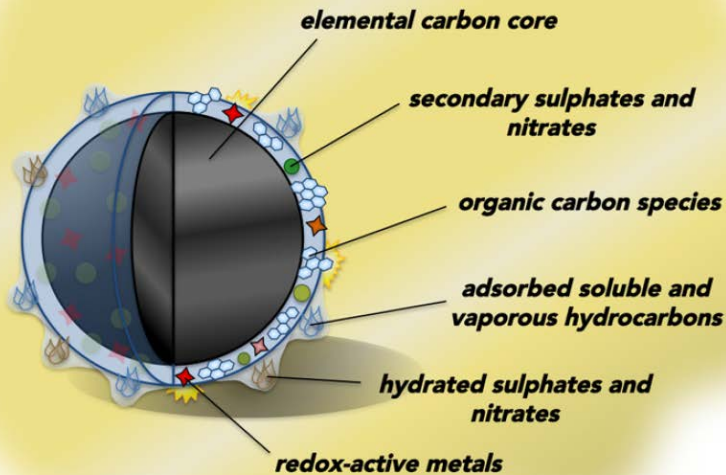
Aeroallergen



Salt

Richards 1997

“Combustion derived nanoparticles“



“Coarse PM” < 10 μm (PM_{10})
(Inhalable)

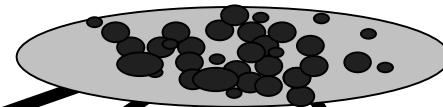
Fine PM < 2.5 μm ($\text{PM}_{2.5}$)
(Respirable)

Ultrafine particles < 0.1 μm
(Nanoparticles)

Toxicological mechanisms?



PM samples collected from different **locations**
(e.g. urban, rural, traffic dominated)
or at different **time points** (e.g. day, season)



Characterization
composition
chemical reactivity

Cell culture systems
(*in vitro* toxicology)

Animal models
(*in vivo* toxicology)

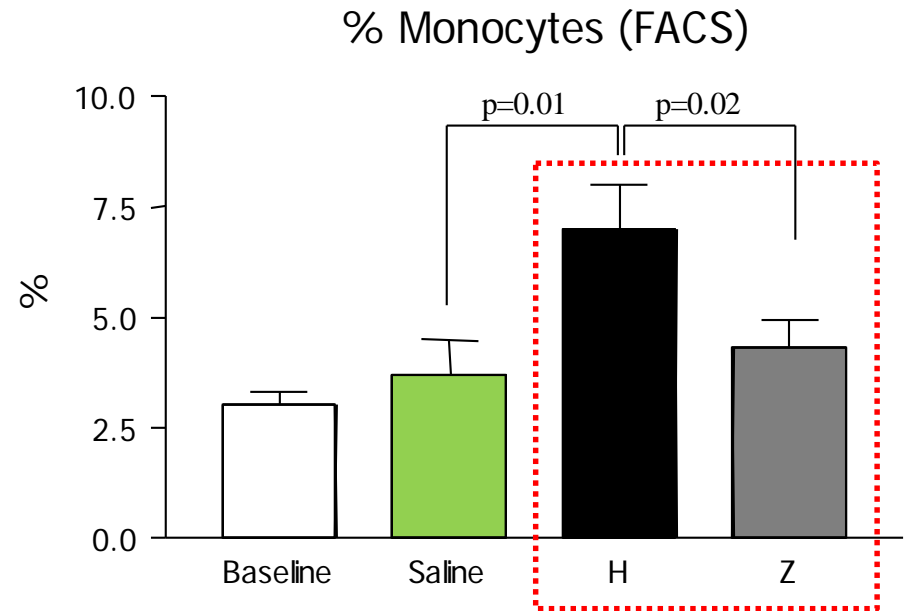
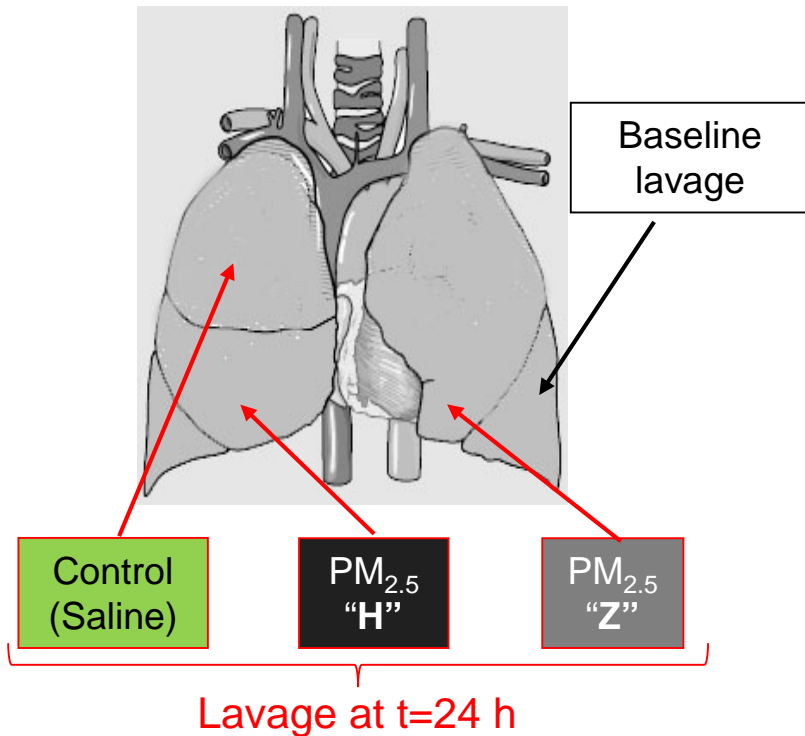
Human studies

Toxicity of PM in human lungs

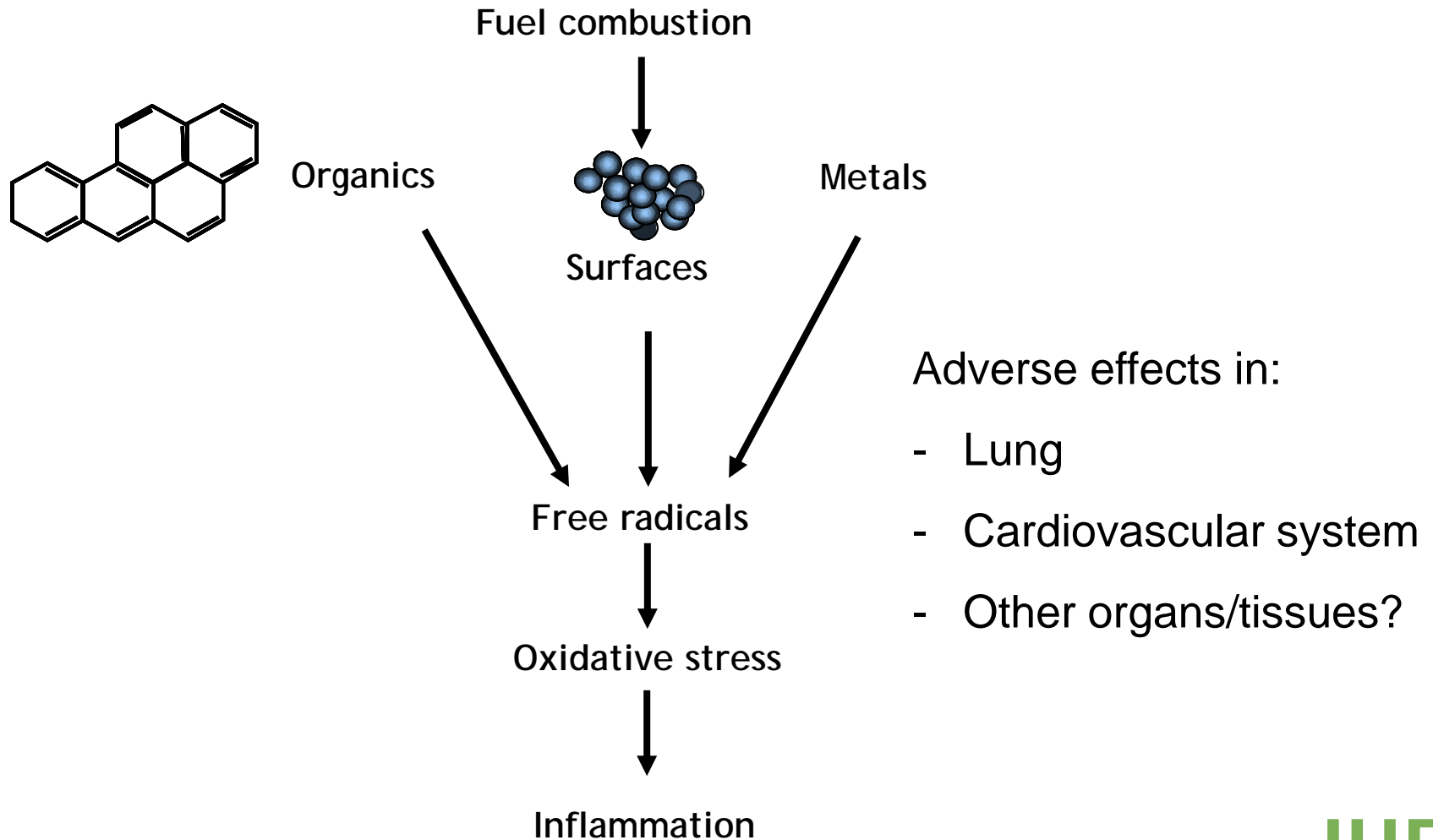
- Sampling of PM at two contrastingly polluted regions:

H (smelter area), Z (non-industrialised)

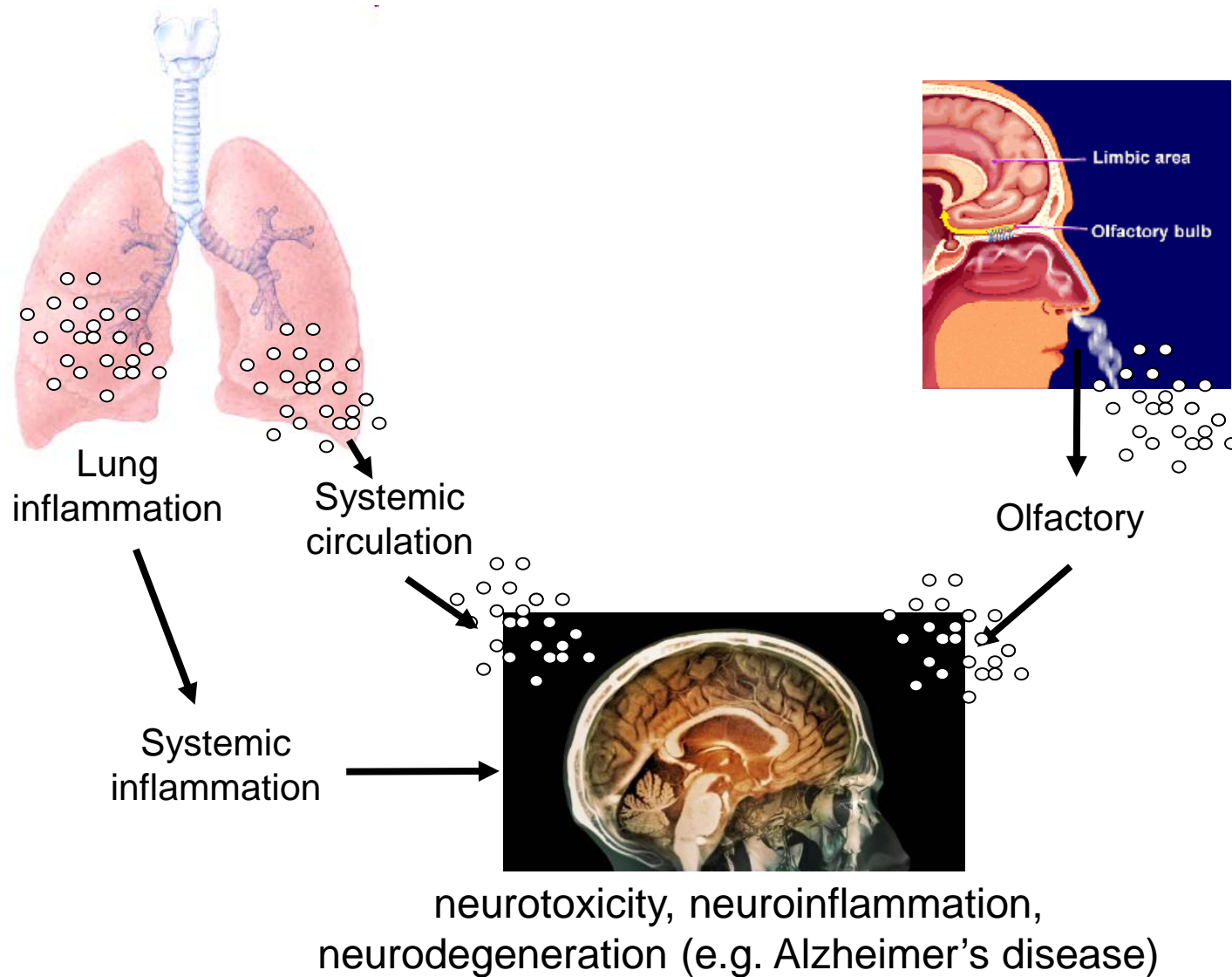
- Segmental instillation of PM_{2.5} for 24 hours in healthy volunteers
- Collection and analysis of inflammation in bronchoalveolar lavage fluid



Oxidative stress and inflammation caused by combustion-derived nanoparticles (< 0.1 μm / 100 nm)



Translocation of ultrafine particles / systemic inflammation



Review

Neurodegenerative and neurological disorders by small inhaled particles

Harm J. Heusinkveld^{a,b,g,*}, Tina Wahle^{a,g}, Arezoo Campbell^c, Remco H.S. Westerink^d, Lang Tran^e, Helinor Johnston^f, Vicki Stone^f, Flemming R. Cassee^{b,d,g}, Roel P.F. Schins^{a,g}

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^c College of Pharmacy, Western University of Health Sciences, Pomona, CA, USA

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^e Institute of Occupational Medicine, Edinburgh, UK

^f Heriot-Watt University, School of Life Sciences, Edinburgh, UK

^g AIR pollutants and Brain Aging research Group

Neurotoxicology. 2016 Sep;56:94-106.

Magnetite pollution nanoparticles in the human brain

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Proc Natl Acad Sci U S A. 2016 Sep 27;113(39):10797-801.

Summary

- PM = complex and heterogeneous mixture
 - ✓ *Organic constituents*
 - ✓ *Metals*
 - ✓ *Ultrafine particles / nanoparticles*
- Local toxicity in the lung (inflammation, lung tissue damage)
- Translocation of ultrafine particles: lung → blood circulation
- Translocation of ultrafine particles to brain:
 - lung → blood → brain*
 - nose (olfactory nerves) → brain*
- Emerging diseases beyond the lung: cardiovascular, brain,..?
- Novel mitigation actions and strategies by regulators and policy-makers?