Health Effects of Particles – Common Projects in Beijing

Wichmann, H.-Erich

Helmholtz Center Munich, Institute of Epidemiology

Workshop on Air Quality and Health in the Greater Area of Beijing HMGU Neuherberg, 19. September 2009
Our Scientific Focus

We want to understand the impact of the environment on health and disease

Medical need driven
- Environmental factors e.g. COPD
- Gene – environment interaction in chronic diseases e.g. Diabetes

Clinical Relevance (evidence based)
Better health decision (treatment & health care)
Better treatment for everybody (new therapies)

Transformation of knowledge from basic research to medical practice: Targets, mechanisms, treatment

HelmholtzZentrum münchen
German Research Center for Environmental Health
Our Institutes and Partners

Universities e.g. TU, LMU

• Pathogenesis of acute myeloid leukemia
• Molecular Oncology
• Osteosarkoma
• Molecular neurogenetics
• Inflammatory lung diseases
• Environmental Dermatology and Allergology
• Immune regulation in childhood
• Hemapoietic Cell Transplants
• Hyperthermia in Tumor Therapy
• Antigen-Specific Immune Therapy
• Pediatric Tumor Immunology
• Innate Immunity in Tumor Biology
• Immune Monitoring

Other Helmholtz-Centers

• Molecular neurogenetics

Companies

• Inflammatory lung diseases

Global network with research institutions

• Immune and Cell Therapy

Allergy

Immune and Cell Therapy

Clinical Cooperation Groups

• Pathobiology
• Toxicology
• Pathology/Tissue banks
• Plant Pathology
• Soil and groundwater ecology
• Health economics
• Epidemiology/Biobanks

Projects

• Inhalation biology
• Comprehensive Pneumology Center

• Stem cells
• Animal models/Mouse Clinic
• Genomics
• Bioinformatics
• Systems biology
• Proteomics
• Structural biology
• Analytics
• Monoclonal antibodies
• Biological and Medical Imaging
• Immune monitoring

HelmholtzZentrum münchen
German Research Center for Environmental Health
Application of epidemiologic and economic methods to understand environmental and genetic influences on human health
Chronic diseases develop and progress
Epidemiology and Health Economics

Lifestyle

Environment

Genetic disposition

Airborne pollutants
Allergens
Nutrients

Respiratory diseases and allergies
Obesity, diabetes and cardiovascular disease
**Epidemiology of allergic diseases**

Two German birth cohorts: GINI + LISA (n=9128)

<table>
<thead>
<tr>
<th>Age</th>
<th>0</th>
<th>0.5</th>
<th>1</th>
<th>1.5</th>
<th>2/3</th>
<th>4</th>
<th>6</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diaries</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Questionnaires</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>House dust</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM exposure</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>
KORA
Collaborative health research in the Region of Augsburg

General structure
- KORA: model of co-financing by partners, in addition to the basis funding of HMGU
- KORA: Custodian for data and biosamples
- KORA-gen: biobank for genetic studies

Resource
- Cohort study (18,000 participants, recruitment age 25 – 74 y)
  Recruitment 1985, 90, 95, 2000; follow-up 1995, 2000, 05, 08
  Interview, questionnaire, physical measurements, blood, urine, DNA
- Myocardial infarction registry (recruitment age < 75 y, since 1985)
Genotyping platform:
- Genome-wide and regional studies (Illumina, Affymetrix, Sequenom)

Sequencing platform:
- (Illumina Genome Analyzer, ABI 48 capillary sequencer)

Metabolomics:
- (API 4000 LC-MS-MS, Hamilton robotics)
Environmental Epidemiology: Particles as a risk factor for cardiovascular diseases

Healthy heart ↔ Occlusion Re-Perfusion

Annette Peters
Times spent in traffic are associated with heart attacks one hour later

- 1466 heart attack survivors
- Adjusted for getting up, strenuous exercise and being outdoors

Update of Peters et al. NEJM 2004
Myocardial Infarction
Gene-environment interaction (EU 6 centers)

- **AIRGENE**: European Multi-center Study in 1003 myocardial infarction survivors (PI: Annette Peters, HMGU)
- 5813 measurements of blood markers of inflammation
- Particulate Matter (PM) and genes involved in regulation of inflammation

> Genetic Susceptibility modifies the influence of PM

![Graph showing change of fibrinogen in PM10 levels](image)

- PM10: Particulate Matter 10
- N=854, N=557, N=264, N=33
- rs1800790 genotype (1: major 2: minor allele)
Exposure characterization relevant for health: Aerosol measurement site in Augsburg

- Personal exposure assessment
- Continuous particle characterisation and innovative chemical characterisation
- Source apportionment
- Development of new measurement techniques
- Characterisation of samples for toxicological experiments
Approach for air pollution research: National and international collaboration

Systemic Inflammation → Atherosclerosis → Heart Attacks

Augsburg study area

Deutsche Forschungsgemeinschaft

EPA Rochester Particle Center

Diabetes

HelmholtzZentrum münchen
German Research Center for Environmental Health
Expected achievements and impacts

- Innovative research to understand the pathomechanisms responsible for early disease onset
- Applied research with respect to an environmental problem
- Advise on measures to reduce ambient particulate air pollution
HMGU-Beijing
Collaborative projects
Study 1: Short-term effects of air pollution on cardiovascular mortality in Beijing

- Funding by the German Research Foundation (DFG), Germany (Funding period: Oct 2005 - Dec 2008).

- Establishing a collaboration between
  - Helmholtz Zentrum München, Munich
  - Helmholtz-Centre for Environmental Research (UFZ), Leipzig
  - Leibniz Institute for Tropospheric Research (IfT), Leipzig
  - Peking University Health Science Center - School of Public Health (Prof. Xiao-chuan Pan).

- Study aims:
  - Analyses of associations between air pollution (gaseous pollutants and particle concentrations in different size fractions from 3nm to 10µm) and daily cardiovascular and respiratory mortality and emergency room visits*.

*results on mortality will be presented by Dr. S. Breitner
Study 2: Health impact of improved air quality during the Olympic Games 2008 in Beijing, China

- Funding by the German Research Foundation (DFG), Germany (Funding period: Sep 2009 - Aug 2012).

- German Research Institutions:
  - Helmholtz Zentrum München, Munich
  - Helmholtz-Centre for Environmental Research (UFZ), Leipzig
  - Leibniz Institute for Tropospheric Research (IfT), Leipzig

- Peking University:
  - Health Science Center - School of Public Health (Prof. Xiao-chuan Pan)
  - College of Environmental Sciences and Engineering (Prof. Tong Zhu).
Aims of the study:

- Assessing the effects of improved air quality before, during and after the 2008 Olympic Games:
  - Impact of concentration reduction of the pollutants PM$_{10}$, PM$_{2.5}$, NO$_2$, and SO$_2$.
  - Impact of particle number concentrations in different size fractions on the association with daily mortality.
  - Quantification of the impact of air pollutants on hospital emergency room visits / hospital admissions.
Aims of the study (continued):

- Analyses of the impact of the changing air quality over a 7-year period (2003-2009) on health.
- Investigating the influences of meteorological conditions.
- Modification of health effects by meteorological conditions (e.g. heat events).
<table>
<thead>
<tr>
<th>Name</th>
<th>Years</th>
<th>Funding/Program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wei Yue (PhD student of Prof. Sheng Wang and Prof. Pan)</td>
<td>2005-2006</td>
<td>Fellowship of the Benz Foundation</td>
</tr>
<tr>
<td>Minjuan Yang (Master student of Prof. Pan)</td>
<td>May – June 2007</td>
<td>-</td>
</tr>
<tr>
<td>Liqun Liu (Master student of Prof. Pan)</td>
<td>Since Oct 2008</td>
<td>University of Munich/China Scholarship Council - Scholarship Program for Chinese PhD-Students</td>
</tr>
<tr>
<td>Jianwei Gu (Master student of Prof. Yuanhang Zhang and Prof. Min Hu)</td>
<td>Since Oct 2008</td>
<td>Helmholtz/ China Scholarship Council - Scholarship Program for Chinese PhD-Students</td>
</tr>
</tbody>
</table>
Study 1: Short-term effects of air pollution on cardiovascular mortality in Beijing

Air pollution data

Network data
Average of 8 sites

IfT data

NO2
SO2
PM10
Meteo
NC
Meteo
Air class
Time series plot of SO₂ for the study period 01.Jan.03 to 30.Apr.05 (network data)
Time series plot of NO$_2$ for the study period 01.Jan.03 to 30.Apr.05 (network data)
Time series plot of $\text{PM}_{10}$ for the study period 01.Jan.03 to 30.Apr.05 (network data)
Meteorological variables
01 Jan. 03 to 30 Apr. 05 (network data)

daily temperature and humidty

+ Temp
+ Humid
Additional air pollution data (IfT Leipzig)

Measurements

Measurement site on the campus of Peking University:

Residential and commercial area with local sources: vehicular traffic, domestic cooking and heating, construction

Wehner et al., EAC 2007
Additional air pollution data (IfT Leipzig)

Measurements

- Sampling on top of a 6-floor building, 20 m above ground
- Number size distributions from 3 nm to 10 μm using Twin DMPS system and APS since March 2004
- This study: March 2004 – Feb 2006

Wehner et al., EAC 2007
Time series of (NC0.003-10) and ratio of NC0.003-0.1 to NC0.003-10 (hourly base) from 04.Mar.04 to 31.12.06
Method: Cluster analysis

- Method for air mass classification
- Dividing the data set into a number of backtrajectory clusters ⇒
  a group of backtrajectories with similar properties is represented by a mean one
  provides a high degree of objectiveness

Here, backtrajectories will be represented by a number of 6 clusters
Air mass classification (II)
March 2004 – February 2006

Cluster analysis

1 - NW slow (94)
2 - N slow (92)
3 - N fast (101)
4 - SE slow (108)
5 - NW fast (92)
6 - S slow (88)

Beijing

Wehner et al., EAC 2007
Frequency of occurrence

Cluster 1  Cluster 2  Cluster 3  Cluster 4  Cluster 5  Cluster 6

Jan  Feb  Mar  Apr  May  Jun  Jul  Aug  Sep  Oct  Nov  Dec

Frequency (%)
Means of $\text{PM}_{10}$ calculated for the 6 clusters of backtrajectories
Mean number size distribution

- 1 - NW slow
- 2 - N slow
- 3 - N fast
- 4 - SE slow
- 5 - NW fast
- 6 - S slow

Wehner et al., EAC 2007
Thank you