Perspectives on 21st Century Air Pollution and Health Research Priorities

Srikanth S Nadadur, PhD
Program Director
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
Research Triangle Park, NC
nadadurs@niehs.nih.gov
27 Institutes and Centers in National Institutes of Health (NIH)
Mission: To discover how the environment affects people in order to promote healthier lives.

Vision: To provide global leadership for innovative research that improves public health by preventing disease and disability
Outline

• Historical overview

• What do we know about Particulate Matter (PM) health effects

• Air pollution health knowledge gaps and future research priorities

• Ongoing collaboration with India on air pollution health research
Where we started?

Pittsburgh, PA
1950

Donora, PA
1948

Los Angeles, CA
1980
Air Pollution Regulation in the USA

**Criteria Pollutants:**
- Particulate Matter
- Ozone
- Nitrogen Oxides
- Sulfur Oxides
- Carbon Monoxide
- Lead

**Hazardous Air Pollutants:**
~189 Toxic chemicals

- The Clean Air Act passed in 1963
- US EPA established in 1970
- National Ambient Air Quality Standards (NAAQS)

Review on a periodic basis (every 5 years)

**Maximum Achievable Control Technology (MACT)**
PM is a complex mixture of solid, semi-volatile and aqueous materials of various sizes found in the air.
Size Distribution of Combustion Generated PM

Whitby, 1978
US EPA, 2004
$\text{PM}_{10}$ Levels Correlate with Hospital Admissions for Pneumonia & Pleurisy; Bronchiolitis & Asthma

**PM$_{10}$ Concentrations, Lindon Site**

**Monthly Bronchiolitis & Asthma Hospital Admissions: All Ages**
Harvard Six Cities Study: Adjusted Mortality Rate Ratios

Portage (P), Wisconsin; Topeka (T), Kansas; Watertown (W), Massachusetts; St. Louis (L), Missouri; Harriman (H), Tennessee; and Steubenville (S), Ohio

Dockery et al., 1993
The overall cohort study evidence demonstrates that a 10-μg/m3 increase in PM2.5 exposure is in general positively associated with excess mortality, largely driven by increases in cardiopulmonary or cardiovascular deaths.
Modified from Brook et al, 2010
<table>
<thead>
<tr>
<th>Health Outcomes Associated with PM 2.5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pulmonary</strong></td>
</tr>
<tr>
<td>Asthma exacerbations, ER visits, hospital admissions, upper and lower respiratory infections</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
</tr>
<tr>
<td>Systemic inflammation, Atherosclerosis, BP, Vascular function, Heart rate variability</td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
</tr>
<tr>
<td>Diabetes, Increased insulin resistance in adipose, Impaired hepatic glucose metabolism, obesity</td>
</tr>
<tr>
<td><strong>Immune</strong></td>
</tr>
<tr>
<td>Impaired T cell function, Inflammation</td>
</tr>
<tr>
<td><strong>Neurological</strong></td>
</tr>
<tr>
<td>Increased incidence of autism (Traffic), Neuro-inflammation</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
</tr>
<tr>
<td>Pre-term birth, Low birth weight</td>
</tr>
</tbody>
</table>

We need deeper understanding to derive biological basis for these observed effects.
Ultrafine Particles

Larger surface area

Oberdorster et al., 2005
What else we know from Engineered Nanomaterials?

- Dissolution of adsorbed constituents (PAHs)
- Potential bio-corona formation
- Persistence and translocation

Sokolov et al., 2015

Bio-Corona formation on engineered nanoparticles

PM 2.5 = agglomerates of UFP
Insights on wood combustion generated proinflammatory ultrafine particles (UFP)

Emanuela Corsini\textsuperscript{a,*}, Senem Ozgen\textsuperscript{b}, Angela Papale\textsuperscript{a}, Valentina Galbiati\textsuperscript{a}, Giovanni Lonati\textsuperscript{b}, Paola Fermo\textsuperscript{c}, Lorenza Corbella\textsuperscript{c}, Gianluigi Valli\textsuperscript{d}, Vera Bernardoni\textsuperscript{d}, Manuela Dell’Acqua\textsuperscript{d}, Silvia Becagli\textsuperscript{e}, Donatella Caruso\textsuperscript{f}, Roberta Vecchi\textsuperscript{d}, Corrado L. Galli\textsuperscript{a}, Marina Marinovich\textsuperscript{a}

Tox Lettrs. 2017

Found qualitatively different protein absorption profiles on beech wood, Conifer and Diesel exhaust UFPs

Increased ultrafine particles and carbon monoxide concentrations are associated with asthma exacerbation among urban children

Kristin A. Evans\textsuperscript{a}, Jill S. Halterman\textsuperscript{b}, Philip K. Hopke\textsuperscript{c}, Maria Fagnano\textsuperscript{b}, David Q. Rich\textsuperscript{a,*}

Env. Res. 2014
What We know about PM Health Effects?

• Epidemiological studies on PM showed positive association with pulmonary, cardiovascular health effects.

• Accumulated knowledge from population studies also show exacerbation of pre-existing disease conditions
  – Asthma, COPD, CVD, Diabetes, metabolic syndrome,

• Associations with pre-term birth, low birth weight

• Laboratory studies using animal models provided some supportive evidence to these observed effects
  – But are questioned due to high dose exposures used
  – Translation of this information to human health effects

• Recent studies show positive association for UFPs
PM Health Effects- What we don’t Know?

- What constituents within PM are causing these observed effects?
- What’s the role of other air pollutants/confounders?
  - How the biological system is perturbed or reacts at the cellular and molecular organization?
    - Acute and chronic effects

Twenty first Century Environmental Health research needs a Paradigm shift?
# The Complex Realities of Exposure

<table>
<thead>
<tr>
<th>Stressor:</th>
<th>Physical, Chemical, Biological, Psycho-social</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source:</td>
<td>Air, Water, Soil, Food, Consumer Products, Drugs</td>
</tr>
<tr>
<td>Place:</td>
<td>Home, School, Work, Neighborhood, Community, City, State, Region</td>
</tr>
<tr>
<td>Time:</td>
<td>Fetal, Child, Adolescent, Young Adult, Adult, Older-adults, Elderly</td>
</tr>
<tr>
<td>Route of Contact:</td>
<td>Skin, Lungs, Diet</td>
</tr>
<tr>
<td>Distribution:</td>
<td>Lungs, Neuro, Skin, GI, other organs</td>
</tr>
<tr>
<td>Targets:</td>
<td>Biological pathways</td>
</tr>
</tbody>
</table>

Exposome
There are multiple conceptualizations of the EXPOSOME...

<table>
<thead>
<tr>
<th>Conceptualization</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wild</td>
<td>All life-course environmental exposures from prenatal period onwards; includes internal body processes, external exposures, and lifestyle factors.</td>
</tr>
<tr>
<td>Rappaport and Smith</td>
<td>Total exposures throughout life, where the “environment” is the body’s internal chemical environment and “exposures” are all the biologically active chemicals in this internal environment.</td>
</tr>
<tr>
<td>Buck Louis</td>
<td>Mixture of environmental exposures, including man-made and naturally occurring chemicals, physical agents (e.g., noise, vibration, temperature), macro level factors (e.g., population density, sanitation), and lifestyle factors.</td>
</tr>
<tr>
<td>Miller</td>
<td>The cumulative measure of environmental influences and associated biological responses throughout the lifespan including exposures from the environment, diet, behavior, and endogenous processes.</td>
</tr>
<tr>
<td>NRC Report</td>
<td>“Eco-exposome” extends concept from point of contact between stressor and receptor, inward into organism and outward to general environment.</td>
</tr>
</tbody>
</table>

.....developing a unifying conceptual framework.
Emerging efforts at NIH: Personal exposure assessment
Comprehensive survey of biological processes
&
Integration of health data
Sensors for Analysis of Chemical Exposures

Personal Monitor for Black Carbon
Columbia University
Steven Chillrud

Personal Ultrafine Particle Sensor
University of Cincinnati
Sang Young Son

A Personal Aerosol Sensor for Children’s Asthma
RTI International

Wearable Sensor for Pesticide Exposures
FLIR, formerly ICx Technologies
Markus Erbeldinger, PI

RAPID Allergenic Particle Identification
Columbia University
Ken Shepard

A Colorimetric Array VOC Dosimeter
University of Illinois at Urbana-Champaign
Kenneth S. Suslick

Nanosensor for Diesel and Gasoline Exhaust
UC Riverside
Ashok Mulchandani

A Real-time Sensor System for Volatile Compounds
Arizona State University
N.J. Tao
Passive sampler wristbands – Volatile organic chemicals

An integrated mobile exposure devise
Location-GPS
Lung function-spirometry
Smart phone tracking

Columbia birth cohort
Beyond Toxics- industrial neighborhood

Kim Anderson, Oregon State University

- Wearable and stationary sensors
- To monitor pediatric environmental exposures, physiological signals, activity, and/or behavior in a natural environment
- To gain insights into environmental determinants of asthma.
- Plug and play physically or wirelessly with the informatics platforms being developed in PRISMS
Multi-hit, Resilience, Acute and Chronic Inflammation

Chronic Inflammation is implicated in diverse diseases

Adapted from:
McCall et al., 2011
Serhan & Petasis, 2011
Air Pollution & Morbidity

• Identify common mechanism(s) across diseases
  – Mediators/players involved in exacerbations (asthmatic, hypertensive, diabetic, etc.,)

• Influence of air pollution constituents
  – Perturbations at cellular and molecular level

• Susceptibility factors
  – Genetic, epigenetics, microbiome

• Biomarkers of exposure/response
Develop Comprehensive Health Knowledgebase

Genomics: What has the potential for happening

Transcriptomics: What appears to be happening

Proteomics: What makes it happen

Epigenomics: How environment influences transcription

Systems biology/Multi-omic Integration

Translational Control: How environment influences translation

Phenomics: Why we care

Metabolomics: What is happening
Analytical Resources & Large Cohorts
Children’s Health Exposure Analysis Resource (CHEAR)

Goal 1
Advance understanding of the impact of environmental exposures on children’s health and development

Goal 2
Provide infrastructure for adding or expanding exposure analysis to studies involving research in children’s health

Composed of a National Exposure Assessment Laboratory Network (6 laboratories), 1 Data Repository, Analysis, and Science Center, and 1 Coordinating Center
Investigate the longitudinal impact of pre-, peri-, and postnatal environmental exposures on pediatric development and health outcomes.

Pediatric cohorts of ~50,000

Focus areas:
- Upper and lower airway
- Obesity
- Neurodevelopment
- Positive Health
Precision Medicine Initiative

All of US Research Program

Data & Research Center
Participant Technologies Center
Health Care Provider Organizations
Bio Bank
All of US Research Program

- Recruit one million or more volunteers
- Develop one of world’s largest biomedical database
  - Reflect country’s rich diversity
- To inform many research studies on a wide variety of Conditions
  - Build Community of participants and empower them with data to improve their own health

- Develop ways to measure risk for a range of disease
  - Environmental exposures, genetic factors and their interactions
- Identify sex-based differences in disease development
- Identify causes for individual differences
- Discover biological markers to predict risk
AP- Health: Integration of Exposure and Health Data

- Biological response profiles
- Wearable sensors
- Networked monitors & remote sensing
- Smartphones & smartwatches
- Data mining Health Outcomes predictions
- Google Maps: GIS layers Organized by Geographical Positioning
- Transportation
- Land Use
- Census Tracts
- Structures
- Postal Codes
- Raster Imagery
- Crowdhsourcing

- Exposure Survey Questionnaire

- Air Quality
- 69
Office Visit for Counselling...

Comprehensive, personal health, medication use, diet, activity, and exposure data
Summary

• Air pollution health research priorities are aimed at:

• Gaining comprehensive understanding of air pollution health effects
  – at individual level
  – By integration of exposure and response phenotypes
  – Generate biological and exposure data through high throughput technologies to monitor initiation and progress of disease
  – Computational predictive modeling approaches to identify common elements across disease and response phenotypes

• Translate this info to assess individual risk and personalized prevention strategies
Air Pollution in Asia

New Delhi - Nov 08, 2016

Beijing, Jan 6, 2016

Ulaanbaatar, Mongolia
Communities of Researchers

- Air pollution public health
  - Epidemiological, clinical, and basic research
- Exposure assessment
  - Satellite, central and personal monitoring tools, and modeling
- Training
  - Council of Scientific and Industrial Research
  - Indian Council of Medical Research
  - Indo US Science and Technology Forum
Workshop to Explore Bilateral Research Opportunities to Address Air Quality and Health Issues
Nov 8-10, 2016
Thank you