Global Environmental Health at NIEHS

Gwen W. Collman, Ph.D.
Director, Division of Extramural Research and Training
National Institute of Environmental Health Sciences

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Today’s Talk

• Global Environmental Burden of Disease
• Environmental Exposures of Interest
• Global Environmental Health (GEH) at NIEHS
• Examples of NIEHS-Funded GEH Research
• Building GEH Research Capacity
• Wrap-up
Global Environmental Burden of Disease
Lancet Commission on Pollution and Health

- Pollution is the leading environmental cause of disease and premature death
- Accounts for 16% of all deaths worldwide
- Exposure to contaminated air, water, and soil across the life-span
- Cost of inaction is high, while solutions yield economic gains

Landrigan et al., Lancet, 2017
23% of all global deaths are linked to the environment — that’s roughly 12.6 million deaths a year.
Children are Especially Vulnerable

Environmental exposures start in the womb, and can have effects throughout life.

Each year 1.7 million deaths of children under 5 are linked to the environment.

- **570,000 deaths** -- Respiratory infections, including pneumonia
- **360,000 deaths** -- Diarrhoea
- **270,000 deaths** -- Neonatal conditions, including prematurity
- **200,000 deaths** -- Unintentional injuries, such as burns, drowning
- **200,000 deaths** -- Malaria

26% of these deaths are preventable.

Adapted from WHO
Environmental Exposures of Interest
How the Environment Impacts Our Health

People are exposed to risk factors in their homes, work places, and communities:

- Air Pollution
  - Including indoors and outdoors

- Inadequate Water, Sanitation
  - And hygiene

- Chemicals
  - And biological agents

- Radiation
  - Ultraviolet and ionizing

- Community Noise

- Occupational Risks

- Built Environments
  - Including housing and roads

- Climate Change

- Agricultural Practices
  - Including pesticide-use, waste-water reuse

Adapted from WHO
Multiple Chemical Exposures

Woodruff, Zota, & Schwartz, Environ Health Perspect, 2011
Slide courtesy of A. Zota
Effects of Developmental Exposures are Lifelong

Early life is a time of vulnerability to environmental exposures, but it also presents an opportunity to intervene to prevent disease.
The Complexities of Documenting Exposures

**Classes:**
- Physical
- Chemical
- Biological
- Psycho-social

**Sources:**
- Air
- Water
- Soil
- Food
- Consumer Products
- Medicines

**Places:**
- Home
- School
- Work
- Community
- City
- State
- Region

**Time:**
- Fetal
- Child
- Adolescent
- Young Adult
- Adult
- Elderly

**Targets:**
- Lungs
- Neuro
- Skin
- GI
- through biological pathways

**Contact:**
- Skin
- Lungs
- Diet

**Cells**

**Blood/Tissues/Organs**

**Populations and Individuals**

**Built Environment, Activities, Behavior**

**Community**

**Region / Ecosystem**
Global Environmental Health at NIEHS
Global Environmental Health (GEH) at NIEHS

• NIEHS recognizes that environmental health problems transcend national boundaries

• The NIEHS GEH program supports research, education, research translation, and training and capacity building in foreign countries

• Overarching goal to reduce environmental health disparities and help vulnerable populations around the world live healthier lives
GEH Focus Areas

**Research**
- Health effects and exposure assessment
- Special emphasis on populations in low- and middle-income countries

**Research Translation**
- Translate research results into information leaders, decision makers, and individuals can use to improve health

**Training and Capacity Building**
- Support international training programs
- Partner with international institutions
- Support GEOHealth Program to build research capacity
GEH Research Focus Areas

- Climate Change
- Children’s Health
- E-Waste
- Cookstoves and Household Air Pollution
- Oceans and Human Health
- Training and Capacity Building
Current GEH Study Locations
As of March 2018

Map showing current GEH study locations around the world, with specific countries shaded to indicate the number of projects (1-5, 6-9, 10-13, 14-19, 20+).
Current GEH Research: Exposures Studied

- Metals: 51
- Air Pollutants: 28
- Mixtures: 22
- Other: 21
- Pesticides: 16
- Chlorinated Compounds: 16
- Hormonal Mimics / Hormones: 13
- Fluorinated Compounds: 11
- Nutrition / Diet: 10
- Psychosocial Stress: 8
- Supplements: 4
- Herbicides / Fungicides: 4
- Extreme Weather / Climate Change: 3
- Pharmaceuticals: 3
- Infectious Agents: 3

Number of Projects
Current GEH Research: Metals Studied

- Arsenic: 28 projects
- Lead: 11 projects
- Manganese: 10 projects
- Mercury: 8 projects
- Cadmium: 8 projects
- Chromium: 2 projects
- Zinc: 2 projects
- Nickel: 1 project
- Copper: 1 project
Current GEH Research: Health Outcomes Studied

- Neurological / Cognitive: 35
- Metabolic: 28
- Cardiovascular: 15
- Respiratory: 12
- Immune: 10
- Thyroid Dysfunction: 8
- Cancer: 6
- Birth Outcomes: 6
- Reproductive: 5
- Microbiome: 5
- Morbidity / Mortality: 4
- Kidney: 4
- Liver: 3
- Skin: 1

Number of Projects
Current GEH Research: Lifestage at Exposure

- **Prenatal / Pre-Conception**: 55 projects
- **Infant (0-1 year)**: 15 projects
- **Youth (1-18 years)**: 27 projects
- **Adulthood (18 years +)**: 18 projects
GEH Training and Capacity Building Grants

- GeoHealth Hubs (U01/U2R): 14
- K99/R00: 9
- Career Awards: 5
- Fellowships: 4
- NCD Research Training: 1
Examples of NIEHS-Funded GEH Research
Pesticides Linked to Neurobehavioral Effects in Ecuadorian Children

- Researchers examined 308 children, 4 to 9 years old, living in flower farming communities in Ecuador
- Conducted behavioral tests between 63 and 100 days after Mother’s Day
- Children tested closer to Mother’s Day had lower neurobehavioral performance
- Findings suggest that periods of peak pesticide use may transiently affect child neurobehavior

Suarez-Lopez et al., NeuroToxicology, 2017
Prenatal Fluoride Exposure and Child Cognitive Outcomes

- Researchers examined 299 mother-child pairs living in Mexico City.
- Measured fluoride in maternal urine and assessed child intelligence at age 4 and 6-12 years.
- Higher prenatal fluoride exposure was associated with lower intelligence scores at 4 and 6-12 years.
- Maternal exposures were in the range of those reported for other general population samples.

Bashash, Environ Health Perspect, 2017
Maternal Inflammation and Child Autism in Finland

• Researchers studied mother-child pairs in a very large case-control study in Finland

• Measured maternal serum C-reactive protein (CRP) levels, a marker of inflammation, during pregnancy

• Highest CRP levels were associated with a 43% increased risk of childhood autism

• Findings suggest treating maternal immune activation may reduce risk of autism

<table>
<thead>
<tr>
<th>CRP by quintile (mg/dL)</th>
<th>OR (95% CI)</th>
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<tbody>
<tr>
<td>0.10 – 0.92</td>
<td>1</td>
</tr>
<tr>
<td>0.93 – 1.77</td>
<td>0.97 (0.68 – 1.37)</td>
</tr>
<tr>
<td>1.78 – 3.18</td>
<td>1.21 (0.86 – 1.69)</td>
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<tr>
<td>3.19 – 5.83</td>
<td>1.21 (0.86 – 1.69)</td>
</tr>
<tr>
<td>5.84 – 88.9</td>
<td>1.43 (1.02 – 2.01)</td>
</tr>
</tbody>
</table>

Maternal early gestational CRP levels by quintile and childhood autism

Brown et al., Molecular Psychiatry, 2014
HEALS has directly linked arsenic exposure to negative influences on human health, including:

- Increased overall mortality
- Impaired neurodevelopment and motor function in children
- Cardiovascular disease and impaired lung function in adults
- Gene-environment interactions related to blood pressure and cardiovascular health
- Gene-environment interactions related to skin lesions

Since 2000, the HEALS cohort has grown to include 35,000 residents from Araihazar, Bangladesh

A HEALS participant (center) and her family and neighbors stand behind a well that has been painted red to warn that the water has high levels of arsenic.
School-Based Educational Intervention Reduces Arsenic Exposures in Bangladesh

- Chronic exposure to arsenic in well water is ongoing in Bangladesh

- Many Bangladeshis have not switched to low-arsenic wells, even though they are available

- Researchers trained teachers to educate 8-11 year old children about risks of arsenic exposure

- Families with the intervention were five times more likely to switch to a safer well, confirmed by reduced urinary arsenic levels

Teaching elementary schoolers to drink from safe water wells becomes a lesson the whole family learns

Khan et al., EHP, 2015
Cognitive and Motor Performance in Congolese Children with Konzo

• Konzo is an irreversible motor neuron disease associated with the consumption of cassava

• Researchers assessed cognitive and motor performance in children with and without konzo during 4 years of follow-up

• Children with konzo had worse motor and cognitive proficiency than those without the disease

• Cognitive effects were observed in children without physical symptoms of konzo, suggesting a subclinical form of the disease

Principal Investigator, Dr. Desire Tshala-Katumbay, observes Congolese women soaking cassava to remove toxins that could trigger paralysis and undermine cognition

Boivin et al., Pediatrics, 2013
Boivin et al., Lancet Glob Health, 2017
Household Air Pollution Investigation Network (HAPIN) Trial

- Randomized, controlled field trial of liquified petroleum gas (LPG) stove and fuel intervention on health across the lifespan
- Includes 3,200 households in four countries: Guatemala, India, Peru, Rwanda
- Monitor stove use and personal exposure to household air pollution, and health outcome assessments
- NIEHS is one of six NIH ICs supporting HAPIN Trial (led by NHLBI)
HAPIN Trial Study Design

**Pregnant Women**
- N=800 Rwanda
- N=800 India
- N=800 Peru
- N=800 Guatemala

**Older Adult Women**
- N=200 Rwanda
- N=200 India
- N=200 Peru
- N=200 Guatemala

**Index Child**
- N=800 Rwanda
- N=800 India
- N=800 Peru
- N=800 Guatemala

- Baseline assessment
- Households randomized to intervention (n=1600) or control (n=1600)
- Followed for 30 months

**Primary outcomes**
- Birth weight
- Child pneumonia (0-2 years)
- Child linear growth (0-2 years)
- Blood pressure in older adult women

**Secondary outcomes**
- Maternal hypertension and pre-term birth
- Fetal growth
- Gross motor development
- Adult chronic diseases

**Followed for 24 months**
Data Across Life Cycle: From Fetal Growth to Adult Outcomes

ADULT OUTCOMES:
• Pollutant exposures and blood pressure/SGRQ at baseline and 1-3, 3-5, 12, 18-24, and 30 months post-randomization
• BART and CIMT at baseline and 18-24 months post-randomization

PREGNANCY AND FETAL GROWTH:
• Fetal ultrasound and pollutant exposures at <20 wk, 24-28 wk, and 32-36 wk
• Birthweight, other maternal outcomes

GROWTH AND HEALTH:
• Quarterly anthropometry
• IYCF and milestones
• Weekly surveillance for pneumonia symptoms and lung ultrasound for imaging
• Pollutant exposures at 6 mo and 12-18 mo
Building Global Environmental Health Research Capacity
Global Environmental and Occupational Health Program (GEOHealth)

- Supports low- and middle-income (LMIC) institutions to serve as regional hubs for collaborative GEH research, data management, training, curriculum development, and policy support
- Supports two linked awards to an LMIC institution for research and a U.S. institution for training
- Funded by FIC, NIEHS, NIOSH, and NCI

GEOHealth Priority Areas
- Agricultural health
- Air quality
- Climate change
- E-waste
- Extractive industries
- Food safety
- Informal work
- Occupational health
- Toxic waste
- Water quality
- Workplace safety
WHO-NIEHS Collaborating Centre

- NIEHS was designated a WHO Collaborating Centre for Environmental Health Sciences in September 2013

- The Collaborating Centre provides a focal point for NIEHS GEH research and new opportunities for translating research findings

- NIEHS assists WHO by:
  - Promoting international research collaborations
  - Raising global awareness of emerging issues
  - Supporting education and training in environmental and occupational health sciences
WHO-NIEHS Collaborating Centre

Focus Areas

- Children’s environmental health
- Influence of environment on non-communicable diseases
- Health effects of climate and weather extremes
- WHO Chemical Risk Assessment Network

Cross-Cutting Focus Area Topics

- Developmental origins of health and disease
- Chronic kidney disease of unknown origin
- E-waste
- Indoor air
Network of WHOCCs for Children's Environmental Health

NIEHS helped establish a network of designated WHO Collaborating Centres that is working to address children's environmental health issues at the local, regional, national, and international levels.
### Global Health Funding Opportunities From NIH

<table>
<thead>
<tr>
<th>FOA Title</th>
<th>FOA #</th>
<th>Eligibility Requirements</th>
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<tbody>
<tr>
<td>Global Brain and Nervous System Disorders Research Across the Lifespan (R21)*</td>
<td>PAR-17-313</td>
<td>Collaboration between LMIC and U.S./upper middle-income institutions</td>
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<td>Global Brain and Nervous System Disorders Research Across the Lifespan (R01)*</td>
<td>PAR-17-314</td>
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<td>Global Infectious Disease Research Training Program (D43)</td>
<td>PAR-17-057</td>
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<td>Mobile Health: Technology and Outcomes in Low and Middle Income Countries (R21 Clinical Trial Optional)</td>
<td>PAR-18-242</td>
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<tr>
<td>International Bioethics Research Training Program (D43)</td>
<td>PAR-16-454</td>
<td>Collaboration between LMIC and U.S. institutions</td>
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<td>Infrastructure Development Training Programs for Critical HIV Research at Low- and Middle-Income Country Institutions (G11)</td>
<td>PAR-16-280</td>
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<tr>
<td>Fogarty HIV Research Training Program for Low-and Middle-Income Country Institutions (D43)</td>
<td>PAR-16-279</td>
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<tr>
<td>Planning Grant for Global Infectious Disease Research Training Program (D71)</td>
<td>PAR-17-058</td>
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## Global Health Funding Opportunities From NIH (cont.)

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<th>FOA Title</th>
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<th>Eligibility Requirements</th>
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<tr>
<td>International Research Ethics Education and Curriculum Development Award</td>
<td>PAR-16-081</td>
<td>Collaboration between LMIC and high-income country institutions</td>
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<td>(R25)</td>
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<tr>
<td>International Research Scientist Development Award (IRSDA) (K01 Independent Clinical Trial Required)</td>
<td>PAR-18-540</td>
<td>U.S. only</td>
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<tr>
<td>International Research Scientist Development Award (IRSDA) (K01 Independent Clinical Trial Not Allowed)</td>
<td>PAR-18-539</td>
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<tr>
<td>Emerging Global Leader Award (K43)*</td>
<td>PAR-17-001</td>
<td>LMIC only</td>
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<tr>
<td>Planning for Non-Communicable Diseases and Disorders Research Training Programs in Low and Middle Income Countries (D71)</td>
<td>PAR-17-097</td>
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*NIEHS-supported funding opportunity
Wrap-Up

- Environmental risks cause millions of deaths and diseases every year.
- People living in low resource countries bear the greatest burden of environmental disease.
- Healthier environments can save lives and prevent disease.
- NIEHS is committed to reducing environmental health disparities worldwide by supporting research, education, research translation, and training and capacity building in foreign countries.
Thank You!

Any Questions?
**GEOHealth Program Progression**

- **GEOHealth Planning (R24)**
  - Supported planning for development of GEOHealth Hubs
  - 16 paired awards made between FY2012-2014

- **GEOHealth Hubs (U01, U2R)**
  - Supporting research and research training activities
  - Seven paired awards made in FY2015
“We know that air and water pollution, pesticide exposure, climate change and other environmental and occupational risk factors contribute to the growing burden of noncommunicable diseases in LMICs. These research hubs are designed to develop a critical mass of scientists who can discover how these exposures trigger diseases, identify effective interventions, and spur policy changes that will improve health.”

— Roger I. Glass, M.D., Ph.D.
Director, Fogarty International Center
Venda Health Examination of Mothers, Babies and their Environment (VHEMBE)

- Birth cohort examining health effects of pesticide exposure from indoor residual spraying (IRS)
- Initiated in 2012, researchers recruited 750 pregnant women from the Venda tribe in Limpopo Province, South Africa
- Assessed mother’s reproductive health and child’s health and development
- Will help clarify trade offs between malaria control and health risks of IRS

VHEMBE psychometrician administers a neurodevelopment assessment
DDT/DDE Exposure and Outcomes in Mothers Living in South Africa

- Mothers living in homes sprayed for malaria control had 5-7 times higher DDT/DDE serum levels than those who did not.
- Mothers with higher DDT/DDE serum levels had elevated odds of hypertensive disorders during pregnancy.
- Frequent mopping of household floors was identified as potential intervention for reducing exposure.

Spatial distribution of DDT concentrations in relation to hospital where VHEMBE mothers gave birth.

Gaspar et al., Environ Health Perspect, 2017
Murray et al., Environ Res, 2018
Heart Rate and Occupational Noise Exposure Among E-Waste Recycling Workers in Ghana

- E-waste workers in Ghana were continually monitored for 24 hours for noise exposure and heart rates.
- More than 40% had noise exposures above recommended levels.
- An elevated heart rate was associated with noise exposure.
- Workers also reported symptoms of cardiovascular disease.
- In addition to chemical exposures, noise exposure may affect e-waste workers’ health.


E-waste dismantling activities at the Agbogbloshie e-waste recycling site in Accra, Ghana
Maternal Exposure to Household Air Pollutants and Birthweight in Tanzania

- Tanzanian women are exposed to CO and PM2.5 from indoor cooking with charcoal and kerosene
- Researchers measured personal exposures of 239 pregnant women, and the weight of their newborns
- There was a significant decrease in infant weight with increases in PM2.5 exposure
- Exposures exceeded WHO air quality guidelines

Wylie et al., Indoor Air, 2017
23% of all global deaths are linked to the environment — that’s roughly 12.6 million deaths a year.

8.2 million deaths caused by the environment are due to noncommunicable diseases – most of these deaths are attributable to air pollution.

Healthier environments could prevent the deaths of 1.7 million children under the age of 5 each year.

Environmental risk factors, such as chemical exposures, climate change, and air, water, and soil pollution contribute to more than 100 disease and injury types.

WHO, 2016
Effects of Developmental Exposures are Lifelong