Seventeenth Annual CEET Symposium
Glen Gaulton Auditorium, Biomedical Research Building
Friday, November 18, 2022

Climate Change and Human Health







Perelman SCHOOL OF MEDICINE
UNIVERSITY of PENNSYLVANIA

CEET
CENTER OF EXCELLENCE IN ENVIRONMENTAL TOXICOLOGY

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Center of Excellence in Environmental Toxicology (CEET)

SEVENTEENTH ANNUAL SYMPOSIUM

Climate Change and Human Health

Glen Gaulton Auditorium & Lobby, Biomedical Research Building
Perelman School of Medicine at the University of Pennsylvania
November 18, 2022

Perelman School of Medicine University of Pennsylvania | CEET Center of Excellence in Environmental Toxicology

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Seventeenth Annual Symposium

Climate Change and Human Health

November 18, 2022

7:30AM – 8:30AM	REGISTRATION AND CONTINENTAL BREAKFAST
8:30AM – 8:45AM	**Welcome & Opening Remarks** Trevor M. Penning, PhD The Thelma Brown and Henry Charles Molinoff Professor of Pharmacology Director, Center of Excellence in Environmental Toxicology (CEET)
8:45AM – 9:45AM	KEYNOTE PRESENTATIONS
	"Climate Change and Extreme Weather Events" Michael Mann, PhD Presidential Distinguished Professor, Earth & Environmental Science Director, Penn Center for Science, Sustainability, and the Media
	"Impact of Climate Change" John Balbus, MD, MPH Office of Climate Change and Health Equity Acting Director Office of the Assistant Secretary for Health U.S. Department of Health & Human Services
9:45AM – 10:45AM	POSTER SESSION I with coffee *Odd-numbered posters*
10:45AM – 12:00PM	PANEL DISCUSSION: **Informing Health Care and Public Health Measures** Moderator: Misha Rosenbach, MD Associate Professor of Dermatology
	Panelists: Aubrey Miller, MD, MPH Deputy Director Office of Science, Coordination, Planning, and Evaluation, National Institute of Environmental Health Sciences
	Joseph Leanza, MD Emergency Medicine Physician and Global Health Fellow
	Lily Brown, PhD Assistant Professor of Psychology in Psychiatry Director at the Center for the Treatment and Study of Anxiety
	Saleem Chapman, MPA Chief Resilience Officer, Office of Sustainability, City of Philadelphia
12:00PM – 1:00PM	LUNCH
	ADDRESSING CLIMATE CHANGE THROUGH THE LENS OF ENVIRONMENTAL HEALTH SCIENCES
1:00PM – 1:40PM	*Climate Change Impacts in Environmental Justice Communities* Moderator: Marilyn Howarth, MD Director, CEET Community Engagement Core
	Community Spotlight I: Eastwick (Flooding) Brenda Whitfield, Eastwick Lower Darby Creek Area Community Advisory Group, Eastwick United CDC
	Community Spotlight II: Grays Ferry (Heat Islands) Meeka Outlaw, Residents Organized for Advocacy and Direction (ROAD)

1:40PM – 2:10PM	*Air Pollution and Lung Health* Moderator: Sharon McGrath-Morrow, MD Professor of Pediatrics Robert Gerard Morse Endowed Chair in Pediatric Pulmonary Medicine **Air Pollution, Climate Change, and Human Health: Learning From Our Past, Bettering Our Future** Michelle Bell, PhD Professor of Environmental Health Yale University
2:10PM – 2:50PM	*Windows-of-Susceptibility* Moderator: Marisa Bartolomei, PhD Professor of Cell and Developmental Biology **Greenspace as a Neighborhood Strategy to Improve Maternal and Infant Outcomes in the Era of Climate Change** Heather Burris, MD, MPH Associate Professor of Pediatrics, Neonatology **Impact of Climate Change on the Timing of Menarche** Mary Regina Boland, PhD Assistant Professor of Informatics
2:50PM – 3:50PM	POSTER SESSION II with refreshments *Even-numbered posters*
3:50PM – 4:30PM	*Environmental Neuroscience* Moderator: Sigrid Veasey, MD Professor of Medicine, Division of Sleep Medicine **The Impact of Climate Change on Sleep** Sigrid Veasey, MD Professor of Medicine, Division of Sleep Medicine **Mental Health and Climate Anxiety** Susan Clayton, PhD Professor of Psychology and Environmental Studies The College of Wooster
4:30PM – 5:10PM	*Environmental Exposures and Cancer* Moderator: Ian Blair, PhD A.N. Richards Professor of Pharmacology **Climate Change and Cancer** Leticia Nogueira, PhD, MPH Senior Principal Scientist, Health Services Research American Cancer Society **UV-light and Skin Cancer** Joanna Walker, MD Assistant Professor of Clinical Dermatology
5:10PM – 5:15PM	**Closing Remarks** Trevor M. Penning, PhD
5:15PM – 6:15PM	RECEPTION

WELCOME MESSAGE

Trevor M. Penning, PhD

The Thelma Brown & Henry Charles Molinoff Professor of Pharmacology

Director, Center of Excellence in Environmental Toxicology
Perelman School of Medicine

It is with enormous pride that I welcome you to the Seventeenth Annual Symposium of the Center of Excellence in Environmental Toxicology (CEET), the University of Pennsylvania's Environmental Health Sciences Core Center. Every year, we choose a theme to embrace so that we can learn more about a field and how it might align with the current and future directions of the CEET. This year's theme is *Climate Change and Human Health*.

The public and many organizations have focused attention on reducing the carbon footprint to lower the Earth's temperature without paying attention to the consequential effects of climate change on human health. As weather-related events, such as floods, heat waves, hurricanes, tornados, and forest fires become more extreme, the risk to human health grows, exacerbating existing physical and mental health conditions, threatening our water and food security, and increasing the risk of zoonotic disease. In step with these changes are the need for disaster response preparedness and recovery, and the identification of public health needs and research gaps — which we hope to further highlight and explore in today's sessions.

Keynote presentations from Dr. Michael Mann and Dr. John Balbus will set the stage for dialogue and discussion, followed by a pivotal panel on "Informing Health Care and Public Health Measures," and featured talks on climate change through the lens of Environmental Health Sciences. We will also hear from some of our community partners who already experience the consequences of flooding and heat stress. Our trainees will also have the opportunity to present their research in environmental health sciences. It will be an exciting and informative day and I look forward to your participation.

- Dr. Trevor M. Penning
Director, CEET

KEYNOTE SPEAKER

Michael E. Mann, PhD

Presidential Distinguished Professor, Department of Earth and Environmental Science

Director, Center for Science, Sustainability, and the Media
University of Pennsylvania

Dr. Mann is Presidential Distinguished Professor in the Department of Earth and Environmental Science at the University of Pennsylvania, with a secondary appointment in the Annenberg School for Communication. His research focuses on climate science and climate change. He was awarded the Hans Oeschger Medal of the European Geophysical Union in 2012. He made Bloomberg News' list of fifty most influential people in 2013. He has received the Friend of the Planet Award from the NCSE, the Award for Public Engagement with Science from the AAAS, and the Leo Szilard Award of the American Physical Society. He received the Tyler Prize for Environmental Achievement 2019 and was elected to the U.S. National Academy of Sciences in 2020. He is a Fellow of the AGU, AMS, GSA, AAAS, author of more than 200 publications, numerous op-eds and commentaries, and five books including Dire Predictions, The Hockey Stick and the Climate Wars, The Madhouse Effect, The Tantrum that Saved the World, and The New Climate War.

KEYNOTE SPEAKER

John M. Balbus, MD, MPH

Office of Climate Change and Health Equity Acting Director

Office of the Assistant Secretary for Health (OASH)

U.S. Department of Health & Human Services

Dr. Balbus is the Acting Director of the new Office of Climate Change and Health Equity within OASH. A physician and public health professional with over 25 years of experience working on the health implications of climate change, Dr. Balbus has served as HHS Principal to the U.S. Global Change Research Program and co-chair of the working group on Climate Change and Human Health for the U.S. Global Change Research Program since he joined the federal government in 2009. Before coming over to the new Office, Dr. Balbus served as Senior Advisor for Public Health to the Director of the National Institute of Environmental Health Sciences.

Prior to joining NIEHS, Dr. Balbus was the Chief Health Scientist at the Environmental Defense Fund and an Associate Professor of Environmental and Occupational Health at the George Washington School of Public Health and Health Services. He received his MPH degree from the Johns Hopkins School of Hygiene and Public Health, his MD degree from the University of Pennsylvania, and his undergraduate degree in Biochemistry from Harvard University. He was elected as a member of the National Academy of Medicine in 2021.

INVITED OUTSIDE PANELISTS AND SPEAKERS

Michelle Bell, PhD

Professor of Environmental Health

Yale University

Dr. Michelle Bell is the Mary E. Pinchot Professor of Environmental Health at the Yale University School of the Environment, with secondary appointments at the Yale School of Public Health, Environmental Health Sciences Division, the Yale School of Engineering and Applied Science, Department of Chemical and Environmental Engineering, and the Yale Jackson School of Global Affairs. Her research investigates how human health is affected by environmental conditions, including air pollution and weather. Other research interests include the health impacts of climate change and environmental justice. Much of this work is based in epidemiology, biostatistics, and environmental engineering. The research is designed to be policy-relevant and contribute to well-informed decision-making to better protect human health and benefit society. She is the Director of the EPA-funded Solutions to Energy, AiR, Climate, and Health (SEARCH) Center.

Saleem Chapman, MPA

Chief Resilience Officer

Office of Sustainability,
City of Philadelphia

Saleem Chapman is the City of Philadelphia's Chief Resilience Officer and Director of the Philadelphia Office of Sustainability. Chapman is responsible for the implementation of and reporting on *Greenworks: A Vision for a Sustainable Philadelphia*. He also oversees the City's preparedness for the unprecedented challenge of the climate crisis, creating a more resilient, equitable city for current and future residents. Before joining the City of Philadelphia, Chapman amassed a vast array of experience in the sustainability field, including professional work in urban policy analysis, environmental justice, and sustainable economic development. Saleem holds a Bachelor's in Biomedical Engineering from Drexel University, as well as a Bachelor's in Political Science and a Master's in Public Administration, both from Penn State University.

INVITED OUTSIDE PANELISTS AND SPEAKERS

Susan Clayton, PhD

Whitmore-Williams Professor of Psychology at the College of Wooster

Susan Clayton (B.A., Carleton College; M.S., Ph.D. Yale University) is Whitmore-Williams Professor of Psychology at the College of Wooster. Dr. Clayton studies the psychology of climate change, and people's social and emotional responses to changes in the natural environment. Her recent research has emphasized climate anxiety, people's sense of possibly debilitating worry about impacts of climate change. She co-authored the American Psychological Association (APA) reports on "Psychology and Global Climate Change" and "Psychological Impacts of Climate Change," and was a lead author on the most recent assessment report from the Intergovernmental Panel on Climate Change.

Aubrey Miller, MD, MPH

Deputy Director Office of Science, Coordination, Planning, and Evaluation, National Institute of Environmental Health Sciences (NIEHS)

Dr. Miller is Deputy Director of the new Office of Scientific Coordination Planning and Evaluation (SCOPE) within the Office of the Director for NIEHS. He leads a portfolio of programs involving global environmental health and climate change, disaster research, and environmental toxics, as well as legislative, policy, strategic planning, and coordination of environmental health issues and activities among NIH, U.S. federal agencies, academia, and other stakeholders. His experiences include numerous public health investigations and research studies involving a wide range of occupational and environmental health issues. He has contributed to the leadership and management of numerous disaster responses including the Libby, Montana, Public Health Emergency involving widespread asbestos contamination, Katrina and other major hurricanes, the World Trade Center and anthrax attacks, the Gulf Oil Spill, and the H1N1 influenza, Ebola, Zika, and COVID-19 infectious outbreaks. He Co-Chairs the new NIH Climate Change and Health Initiative to develop needed research, capacity building, and training. He also directs the NIH Public Health Emergency and Disaster Research Response (DR2) Program which focuses on improving disaster research capabilities through enhancing policies, infrastructure, training, and integration of stakeholders, especially academia and impacted communities.

INVITED OUTSIDE PANELISTS AND SPEAKERS

Leticia Nogueira, PhD, MPH

Senior Principal Scientist, Health Services Research

American Cancer Society

Leticia Nogueira, PhD, MPH, is Senior Principal Scientist in the Surveillance and Health Equity Science Department at the ACS. She holds an Adjunct Professor position at the Rollins School of Public Health, Emory University.

Dr. Nogueira's research focuses on disparities in cancer care and outcomes that can be addressed by policy changes, with a focus on climate change and structural racism.

Dr. Nogueira earned her doctoral degree from the University of Texas at Austin and her Master of Public Health from the Harvard School of Public Health. She received the Fellows Award for Research Excellence from the National Institutes of Health in 2014, the Woman in Cancer Research Award in 2013, and the Minority Scholar in Cancer Research Award in 2010, both from the American Association for Cancer Research. In 2018, Dr. Nogueira was inducted into the University of Texas College of Natural Sciences Hall of Honors and in 2020, she received the Outstanding Young Alumni Award from the University of Texas at Austin.

MISSION AND VISION STATEMENT

The Center of Excellence in Environmental Toxicology (CEET) is a school-based center housed in the Perelman School of Medicine at the University of Pennsylvania. As the spectrum of environmental health science is broad, ranging from toxicology, chemistry, environmental science, environmental disease, epidemiology, public health, and policy, its more than 80 members come from 18 departments and 5 schools as well as the Children's Hospital of Philadelphia. CEET is Penn's designated Environmental Health Science Core Center (EHSCC) funded by the National Institute of Environmental Health Sciences (NIEHS).

The CEET elucidates the mechanistic links between environmental exposures and human disease and translates its findings into action to improve the health of vulnerable individuals, and local, national and global communities.

The CEET mission is achieved by both its community-based research model and by its emphasis in thematic areas. The Community Engagement Core (CEC) identifies community-based environmental health problems that are then framed by our Integrative Health Sciences Facility Core (IHSFC) into research questions that can be answered by CEET investigators. Findings are then translated back to the community using a "community-first communication model." An emerging theme is precision public health in which community exposomes can be used to identify sub-populations most vulnerable to air pollution, lung cancer incidence and lead poisoning.

Our flexible thematic areas: Air Pollution and Lung Health; Environmental Exposures and Cancer; Windows-of-Susceptibility; and, Environmental Neuroscience, address immediate concerns that affect our region. Each of these thematic areas embrace exposure assessment, the adverse outcome pathway or network affected and translates these findings to affected communities and human subject-oriented research. In each of these areas, the CEC works with communities impacted by relevant exposures.

The CEET enables its investigators to conduct biomarker work of exposure and effect using its Translational Biomarker Core, which uses sophisticated liquid chromatography mass spectrometry methods. CEET investigators have access to an Exposure Biology Informatics Core so that large siloed data bases in exposomics, genomics, proteomics, metabolomics and chemoinformatics can be merged as predictors of response and disease onset. The Core is also positioned to take these large data sets and use machine learning and AI to predict responses to toxicants. The IHSFC of the CEET provides assistance with a broad range of transdisciplinary services including study design, exposure biology laboratories with access to biospecimens via the Penn Biobank; and biostatistical support.

The CEC works with six communities in Pennsylvania to empower them with new knowledge so that they are better informed to influence decision makers about public health policy. To improve the environmental health of these and similar affected communities, the CEET educates health care professionals (Residency Program in Occupational and Environmental Health, Nursing concentration in Occupational and Environmental Health, and Master of Public Health Programs) to improve public health outcomes.

CENTER OF EXCELLENCE IN ENVIRONMENTAL TOXICOLOGY

Perelman School of Medicine at the University of Pennsylvania

Center Membership

Thematic Area I

AIR POLLUTION AND LUNG HEALTH

Leader: Sharon McGrath-Morrow, MBA, MD

Julian Allen, MD
Andrea Apter, MD
Michael Beers, MD
Ian Blair, PhD
Jason Christie, MD, MSCE
Reto Gieré, PhD
Sarah Henrickson, PhD**
David Hill, MD, PhD**
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Trevor Penning, PhD
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Jessica Rice, DO, MHS**
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Thematic Area II

ENVIRONMENTAL EXPOSURES AND CANCER

Leader: Ian Blair, PhD

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Thematic Area III

WINDOWS-OF-SUSCEPTIBILITY

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Jerome Strauss, MD, PhD
Aalim Weljie, PhD
Rebecca Wells, MD

Thematic Area IV

ENVIRONMENTAL NEUROSCIENCE

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Associate Director, Human Studies Design and Performance Services:
Aimin Chen, MD, PhD

Associate Director, Biostatistics:
Wei-Ting Hwang, PhD

TRANSLATIONAL BIOMARKER CORE

Director: Clementina Mesaros, PhD

*Adjunct Member
**Affiliate Member

CC1 Reducing the Carbon Footprint of Travel to an International Dermatology Conference: A Case Study of the Medical Dermatology Society's Carbon Footprint Program

Annika Belzer, BS[1], Misha Rosenbach, MD[2], Eva R. Parker, MD[3], John S. Barbieri, MD, MBA[4], Caroline A. Nelson, MD, FAAD[5]**

[1]Yale University School of Medicine, New Haven, CT USA; [2]Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA USA; [3]Department of Dermatology, Center for Biomedical Ethics and Society, Vanderbilt University Medical Center, Nashville, TN USA; [4]Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA USA; [5]Department of Dermatology, Yale University School of Medicine, New Haven, CT USA

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Anthropogenic processes have led to at least a 1.0˚C increase in global mean surface temperatures from pre-industrial levels.[1] It is predicted that temperatures will continue to uptrend by an additional 0.5˚C by 2052, leading to significant effects on human as well as planetary health.[1] Despite awareness of the impact of climate change on human health, the healthcare sector continues to produce significant greenhouse gas emissions (GHG).[2] In addition to clinical, research, and pharmaceutical spaces, international medical conferences contribute to healthcare's carbon footprint.[3] Travel is responsible for a large portion of CO2 equivalent (CO2e) emissions from a conference; an analysis of an international conference with nearly 5,000 attendees reported that CO2e emissions from air travel to the conference were equivalent to weekly emissions of 9,366 American households.[3] In 2022, the Medical Dermatology Society (MDS) introduced its Carbon Footprint Program in an effort to minimize the negative impact of the society's Annual Meeting. Attendees were offered an opportunity to purchase carbon offsets, which fund projects that aim to decrease atmospheric CO2 or sequester CO2. We analyzed the carbon footprint of travel to the MDS Annual Meeting in Boston, Massachusetts using data on each attendee's city of origin. Attendees who could drive to the Annual Meeting in three hours or less were included in the ground travel analysis; all other attendees were included in the air travel analysis. Air travel to the meeting led to approximately 291,461 lb of CO2e emissions. Ground travel to the meeting led to between 2,326 (100% train transit) lb and 6,954 (100% car transit) lb of CO2e emissions. $485 were contributed to carbon offsets, reducing the carbon footprint of the Annual Meeting by 48,502 lb. The MDS Carbon Footprint Program demonstrates proof of concept. This program was not financially or logistically burdensome, nor was it time intensive or difficult for attendees to navigate. We believe this model could be expanded to dermatology conferences broadly, placing our field as a leader in sustainability and climate health.

References:
1. doi: 10.1017/9781009157940.001
2. doi: 10.1016/S0140-6736(19)32596-6
3. doi: 10.4269/ajtmh.20-1013

CC2 Effect of Environmental Lighting on Circadian Control of Lung Injury

Oindrila Paul PhD[1], Amruta Naik PhD[1], Kaitlyn Forrest BS1, Lora Assi BA[1], Mahdi Rashidzada[1], Shaon Sengupta MD[1,2]

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Background: Various aspects of our response to infections is under clock control. We have previously shown that circadian rhythms provide a time-of-day specific protection to mice infected with Influenza A virus (IAV)- mice infected at ZT11 had three-fold higher mortality than littermates infected at ZT23. Circadian disruption due to prolonged light exposure is ubiquitous to modern lifestyle. It is not known if perturbation of environmental lighting can disrupt this time-of-day specific protection conferred by the circadian clock.

Objective: Our aim was to determine if exposure to prolonged lighting can reverse the circadian gated protection by worsening lung repair following infection with IAV. Design/Methods 8-16-week-old C57bl/6J mice were infected with IAV at either ZT23 or ZT11. A subset of the group infected with IAV at ZT23, was moved to constant light (LL) on day 4 post-infection (p.i). Weight loss trajectories, clinical scores and mortality were determined. Lungs were harvested for histology and viral titers.

Results: Mice infected at ZT23 and maintained in 12hr LD conditions throughout had better survival than mice infected at ZT11 (Mortality: 12% in ZT23LD vs 55% in ZT11LD; $p<0.01$ logrank test). However, mice infected at ZT23 but moved to constant light later, lost this protection (mortality 42%). Weight loss and clinical scores has similar trend. All groups cleared the virus by day 8-10 p.i. We found mice subjected to constant light p.i. had worse immunopathology on lung histology (day 30) suggesting poor repair.

Conclusion and Significance: We conclude that perturbations in environmental lighting can have profound impact on lung repair, reversing the benefits of robust circadian rhythms preceding infections. These results support efforts to design hospitals and especially ICUs that are aligned with the host's circadian rhythms.

Supported by NHLBI-R01HL155934-01A1 Sengupta (PI); NHLBI-R01HL147472-Sengupta (Co-I)

CC3 Rates of Drug Safety Endpoints Differ by Ambient Temperatures Experienced by Medicaid Beneficiaries with Type 2 Diabetes Mellitus

Kacie Bogar, MS[1], Colleen M. Brensinger MS[1], Sean Hennessy, PharmD, PhD[1,2], James H. Flory, MD, MSCE[1,3], Michelle L. Bell, PhD[4], Christopher Shi[5], Warren B. Bilker, PhD[1], Charles E. Leonard, PharmD, MSCE[1,2]

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As climate change exacerbates the negative effects of extreme ambient temperature on health, there is urgency for personalized diabetes care to consider a person's environment. This is especially true for disadvantaged populations such as Medicaid enrollees, who—due to structural racism and socioeconomic disparities—have a higher prevalence of type 2 diabetes mellitus (T2DM) and may be particularly susceptible to extremes in outdoor temperature and their accompanying adverse health outcomes. Therefore, we examined how extreme temperatures affected the occurrence of 1) serious hypoglycemia, 2) diabetic ketoacidosis (DKA), and 3) sudden cardiac arrest/ventricular arrhythmia (SCA/VA) among Medicaid beneficiaries with T2DM. We conducted an analytic epidemiologic study using 1999–2010 enrollment and healthcare claims data from Medicaid and Medicaid-Medicare dual enrollees from California, Florida, New York, Ohio, and Pennsylvania, linked to publicly-available meteorologic data from the National Oceanic and Atmospheric Administration. Persons with T2DM were identified and followed from the date of T2DM diagnosis through either benefit disenrollment or death, whichever came first. Within this observation time, we calculated crude occurrence rates (and 95% confidence intervals) for three health outcomes of high concern for persons with T2DM—hospital presentation for serious hypoglycemia, hospital admission for DKA, and hospital presentation for SCA/VA—by prespecified strata of maximum daily ambient temperature in degrees Celsius (◦C), from which we generated trendlines with weighted 95% confidence bands. We found differences in rates of health outcomes by daily ambient temperatures experienced by Medicaid and Medicaid-Medicare enrollees with T2DM. For serious hypoglycemia, we found a 'j-shaped' relationship in which rates were highest during cold and hot temperature extremes; the p-value for the quadratic term for maximum ambient temperature was <0.001. For DKA, we found a higher rate during cold (-17.8–-12.2◦C) vs. hot (>43.3◦C) temperature extremes; the p-value for the linear term for maximum ambient temperature was 0.003. For SCA/VA, we found a 'j-shaped' relationship in which rates were highest during cold and hot temperature extremes; the p-value for the quadratic term for maximum ambient temperature was 0.031. Considering patient -experienced ambient temperature may be an essential missing piece to reducing disparities in diabetes-related adverse health outcomes.

Supported by a Quartet Pilot Research Award funded by the Population Aging Research Center at the University of Pennsylvania (Penn). Drs. Leonard and Hennessy are further supported by the following National Institutes of Health (NIH) (R01AG060975, R01DA048001, R01AG064589, R01AG025152, R01AG077620, and R01MH130435) and Centers for Diseases Control and Prevention (CDC) (R01CE003347) grants. Dr. Flory is supported by the following NIH grant: P30CA008748. Mr. Shi's effort was supported by Penn's Undergraduate Clinical Scholars Program: Pathway to Clinical Research Careers, funded by NIH (R25DK108711). The content herein is solely the responsibility of the authors and does not necessarily represent official views of the University of Pennsylvania, NIH, or CDC.

CC4 Toxins Produced by Blue Green Algae Cause Neonatal Extrahepatic Bile Duct Damage

Kapish Gupta[1,2], Rebecca Wells[1,2]

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Neonatal biliary diseases, in particular biliary atresia (BA) are associated with bile duct damage and bile duct fibrosis. Although the cause of BA is unknown, studies have suggested a role for prenatal environment insults including viral infection and toxin exposure. Notably, maternal bile ducts do not appear to be affected. Disturbed glutathione-metabolism appears to play a role in disease progression. Thus, we hypothesized that environmental toxins that alter glutathione-dependent redox homeostasis may cause neonatal biliary disease. To test this hypothesis, we focused on microcystins, a class of toxins from blue-green algae implicated previously in the disruption of glutathione mediated detoxification. We tested 9 commercially available microcystins and discovered that one specific microcystin, microcystin-RR,but not the other microcystins, caused lumen closure in spheroids made using cholangiocytes isolated from 2-day old but not adult mice. Average lumen closure increased with increasing microcystin-RR concentration and exposure time, with ~80% closure at 400 nM microcystin RR within 24 hr of microcystin RR treatment. We further examined the damage in bile ducts isolated from 2-day and 18-day old mice and cultured ex-vivo. We found bile duct occlusion at 400 nM microcystin-RR in ducts from 2-day old mice but no damage in ducts from 18-day old mice. Furthermore, we also found increased vimentin expression on cholangiocytes in ducts (2-day old mice) treated with microcystin-RR, suggesting epithelial to mesenchymal transition. We were able to partially prevent microcystin-RR-induced lumen closure by treating bile ducts with 20 μM N-acetyl cysteine, suggesting a role for redox homeostasis in lumen closure. We conclude that microcystin-RR exposure is a potential cause of neonatal extrahepatic bile duct damage. Additionally, this study also suggests that N-acetyl cysteine could potentially be used in the treatment of neonatal biliary disease.

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CC5 Mapping and Characterizing the Trends of Extreme Heat Events and Heat-Vulnerable Communities in Pennsylvania, USA

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Climate change has intensified and increased the frequency of heat-related events in recent years in many parts of the world, including the United States. As extreme heat events are believed to cause excess human morbidity and mortality, it is essential from the public health perspective to understand the trends and variations of extreme heat events over time and to identify geographic areas subjected to this impact. In particular, whether the areas classified by the Commonwealth of Pennsylvania as environmental justice (EJ) areas are more vulnerable to those heat events is unknown. We hypothesize that communities in those heat intensified areas are heterogeneous regarding sociodemographic characteristics, health behaviors, built environment, and other environmental risk factors or exposures. Thus, suggesting an individualized approach to remediate the impact of climate change may be warranted. In this project, we will utilize data from the CDC's National Environmental Public Health Tracking Network (NEPHTN) to map and characterize the trends of extreme heat events and heat-vulnerable Communities in Pennsylvania, USA. The primary outcome variables will be the number of extreme heat events and extreme heat days at the census tract level. Extreme heat events are periods in which the estimated air temperature at 2 meters above the surface (North American Land Data Assimilation System (NLDAS-2) is above the specified absolute or relative threshold for a duration of at least 2 or 3 consecutive days. The spatial distribution of the number of extreme heat events over the past few decades (up to 1980) will be displayed using choropleth maps. A Line plot will be created to visualize the trend and variation over time. The outcomes of extreme heat events will be analyzed using zero-inflated Poisson regression with random effects (random intercept and/or random slopes) to estimate the trends and produce area-specific predictions via empirical Bayes estimation. Geographic areas with high predicted number of events and/or those with increasing trend/slope will be identified. The trends and trajectories will be summarized and compared between EJ and randomly selected non-EJ areas. Furthermore, we will describe and compare area-level characteristics between those communities with and without increasing trends using descriptive statistics, graphs, and appropriate statistical tests. The census tract or county-level indicators we may analyze will be grouped in to the following four categories: (1) population demographic (e.g., population density, percent of aged >65, median income, education, employment, social vulnerability index, etc.), (2) lifestyle health behavior (e.g., obesity, smoking, alcohol use, physical activities, etc.) (3) built environment (e.g., housing, traffic, internet coverage, medical facilities, flooding preparedness, etc.) (4) environmental exposure (e.g., air quality, acute toxic substances release, etc.).

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CC6 Quantifying Heat-related Illness Morbidity Attributable to Climate Change in North Carolina

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Climate change is known to increase the frequency and intensity of hot days (daily maximum temperature ≥ 30°C), both globally and locally. Exposure to extreme heat is associated with numerous adverse human health outcomes. This study estimated the burden of heat-related illness (HRI) attributable to anthropogenic climate change in North Carolina physiographic regions (Coastal and Piedmont) during the summer months from 2011-2016. Additionally, estimated future HRI morbidity burden attributable to climate change assuming intermediate and higher greenhouse gas emission scenarios. The association between daily maximum temperature and the rate of HRI was evaluated using the Generalized Additive Model. The rate of HRI assuming natural simulations (i.e., absence of greenhouse gas emissions) and future greenhouse gas emission scenarios were predicted to estimate the HRI attributable to climate change. Over four years (2011, 2012, 2014, and 2015), we observed a significant reduction in the rate of HRI assuming natural simulations compared to the observed. About 3 out of 20 HRI visits are attributable to anthropogenic climate change in Coastal (median: 13.40% (IQR: -34.90,95.52)) and Piedmont (median: 16.39% (IQR: -35.18,148.26)) regions. During the future periods, the median rate of HRI was significantly higher (78.65%: Coastal and 65.85%: Piedmont), assuming a higher emission scenario than the intermediate emission scenario. We observed significant association between anthropogenic climate change and adverse human health outcomes. Our findings indicate the need for evidence-based public health interventions to protect human health from climate-related exposures, like extreme heat, while minimizing greenhouse gas emissions.

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AP1 Linking Ambient NO2 Pollution Measures with Electronic Health Record Data to Study Asthma Exacerbations

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Electronic health record (EHR)-derived data can be linked to geospatially distributed socioeconomic and environmental factors to conduct large-scale epidemiologic studies. Ambient NO2 is a known environmental risk factor for asthma. However, health exposure studies often rely on data from geographically sparse regulatory monitors that may not reflect true individual exposure. We contrasted use of interpolated NO2 regulatory monitor data with raw satellite measurements and satellite-derived ground estimates, building on previous work which has computed improved exposure estimates from remotely sensed data. Raw satellite and satellite-derived ground measurements captured spatial variation missed by interpolated ground monitor measurements. Multivariable analyses comparing these three NO2 measurement approaches (interpolated monitor, raw satellite, and satellite-derived) revealed a positive relationship between exposure and asthma exacerbations for both satellite measurements. Exposure-outcome relationships using the interpolated monitor NO2 were inconsistent with known relationships to asthma, suggesting that interpolated monitor data yields misleading results in small region studies.

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AP2 Air Pollution Changes in Philadelphia Following the 2019 PES Refinery Closure

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The Philadelphia Energy Solutions refinery was considered the city's biggest stationary source of air pollution and a notorious toxic emitter. On June 21st, 2019 a corroded pipe led to a fire which resulted in a massive explosion. The facility leaked hazardous chemicals into the surrounding Grays Ferry neighborhood in South Philadelphia, where many residents reported feeling sick in the coming days. Soon after, the refinery was permanently closed. Our research used publicly available data from the EPA to visualize the changes in PM2.5, SO2, and volatile organic compounds (VOCs) in the neighborhood. We created linear regression models and performed statistical analyses to determine the significance of the correlation in pollutant trends and the refinery closure. We examined pollutant trends in Camden, NJ as well to see if any pollutants experienced a short burst in concentration the night of the explosion.

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AP3 Investigating the Role of Serum Amyloid A in Mediating T cell Dysfunction in Pediatric Obese Asthma

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Pediatric obese asthma (OA) is a complex disease at the intersection of two of the most common chronic inflammatory disorders in children. While it is well-established that obesity is associated with increased risk of asthma incidence and that OA patients endure increased severity of asthma symptoms, the immunological mechanisms by which obesity modifies asthma remain poorly understood. We have previously demonstrated CD4 and CD8 T cells isolated from the PBMCs of OA children are skewed towards Th2 and exhausted-like phenotypes, respectively. Given these findings, we sought to better understand CD4 and CD8 T cell function in the context of OA using a mouse model. Using high fat diet to induce obesity and house dust mite to induce asthma, we studied four groups of mice: healthy controls (HC), asthma alone (A), obesity alone (O), and obese asthma (OA). In this study, we demonstrate that non-naïve CD8 T cells isolated from the lungs of OA mice showed increased expression of several activation and inhibitory receptors (PD-1+Eomes+, PD-1+TOX+) compared to healthy controls. Additionally, we found evidence of increased Th2 (CCR4+CCR6-) skewing in the lungs of OA mice. These results recapitulate the phenotypes observed in our human data and provide a reasonable model to interrogate mechanisms of T cell dysfunction in pediatric OA. One candidate mediator of altered CD4 and CD8 T cells responses in OA is Serum Amyloid A (SAA). SAA was recently shown to be critical for Th2 immunity in an HDM model of allergic asthma and has been shown to alter cytokine production by CD8 T cells in vitro. Using both human subjects and mice, we demonstrate that SAA is elevated in the serum of OA individuals compared to HC. Taken together, these data provide preliminary evidence for future studies interrogating a mechanistic linked between SAA and T cell function in OA.

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EEC1 Exploring the Role of Aldo-Keto Reductases in the Metabolic Activation of 6-Nitrochrysene

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As the culprit of 4.2 million premature deaths annually, ambient air pollution is an urgent threat to public health and is predicted to increase as a result of climate change. The lung is particularly susceptible as a site for absorption of air pollutants and damage due to the pulmonary region's large surface area and thin tissues separating inhaled air from the bloodstream. Lung cancer is the world's leading cause of cancer mortality, and in 2010 the World Health Organization attributed approximately 223,000 lung cancer deaths to air pollution. Diesel exhaust is a potent source of carcinogens such as nitrated polycyclic aromatic hydrocarbons (NO2-PAHs). Metabolic activation by nitroreduction and oxidation of NO2-PAHs can intensify the mutagenic and tumorigenic effects of these pollutants. 6-Nitrochrysene, a representative NO2-PAH in diesel exhaust, can undergo nitroreduction to form 6-aminochrysene, that, upon sulfonation or acetylation of a hydroxylamino intermediate, can form carbenium and nitrenium ions that form DNA adducts. 6-Nitrochrysene can also be monooxygenated to form nitrated polycyclic aromatic hydrocarbon dihydrodiols (PAH-DHDs) that have the potential to be oxidized to form a highly reactive nitro-o-quinone. Previous studies from our lab have shown nitroreductase activity of human aldo-keto reductases (AKRs) toward NO2-PAHs such as 6-nitrobenzanthrone and 1-nitropyrene and have also shown dehydrogenase activity of AKRs toward non-nitrated PAH-DHDs. We hypothesize that AKRs mediate the 6-electron reduction of 6-nitrochrysene to 6-aminochrysene and oxidize the dihydrodiols of 6-nitrochrysene. Here, we use discontinuous enzymatic assays monitored by UV-HPLC to establish kinetic parameters for AKRs using 6-nitrochrysene and its dihydrodiols as substrates. Future works include LC-HRMS to confirm product identity and in cell fluorescence assays to determine cellular metabolic activity. The imminent risks from climate change caused by fossil fuel combustion intensifies the need to elucidate the role of environmental agents in pathogenesis, and this study contributes to our understanding of AKR activity in the metabolic activation of air pollutants.

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EEC2 Role of Transfected Human Aldo-Keto Reductases on HPRT Gene Mutagenicity in V79-4 Cells Exposed to Nitroarenesa

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1-Nitropyrene (1-NP), 1,8-dinitropyrene (1,8-DNP), and 3-nitrobenzanthrone (3-nitro-7H-benz[de] anthracen-7-one, 3-NBA) are nitroarenes that are air pollutants found in diesel exhaust and ranked as either group 2A probable or group 2B possible human carcinogens by the International Agency for Research on Cancer. The metabolic activation of these compounds by nitroreduction contributes to the mutagenicity of these compounds. Specifically, the hydroxylamino intermediate can be O-acetylated to result in a good leaving group for the formation of tautomeric nitrenium and carbenium ions that bind guanine of DNA. Aldo-keto reductases (AKR) 1C1-1C3 catalyze the aerobic nitroreduction of 1-NP, 1,8-DNP, and 3-NBA, and NAD(P)H:quinone oxidoreductase 1 (NQO1) also catalyzes the nitroreduction of 3-NBA. The extent to which these enzymes contribute to the mutagenicity of these nitroarenes is unknown. We investigated the mutagenicity of these compounds at the hypoxanthine-guanine phosphoribosyl transferase (HPRT) locus in V79-4 Chinese hamster fibroblasts using 6-thioguanine selection in response to transfected AKR1C1-1C3. Transfection of AKR1C1, AKR1C2, or AKR1C3 plasmid at 2 μg/mL did not cause mutagenicity in the absence of nitroarene exposure. 1-NP at 1, 5, or 10 μM in the absence of AKR1C transfection did not increase mutagenicity relative to vehicle (0.1% DMSO). In the presence of AKR1C1, AKR1C2, or AKR1C3 transfection at 1 or 2 μg/mL, 1-NP at 5 or 10 μM increased mutagenicity relative to the untransfected controls, showing mutagenicity was dependent on AKR1C transfection. 1,8-DNP or 3-NBA at 5 or 10 μM caused mutation in the absence of AKR1C1, AKR1C2, or AKR1C3 transfection; however, 1 or 2 μg/mL of AKR1C1, AKR1C2, or AKR1C3 plasmid increased this mutagenicity. Mutagenicity for 3-NBA in absence of AKR1C can be attributable to NQO1 present in V79-4 cells; however, the enzymes involved in 1,8-DNP nitroreduction in the absence of transfected AKR1C are unknown. Our study shows that transfection of human AKRs is sufficient to cause mutation by nitroarenes at the HPRT gene locus.

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WS1 Mechanisms by Which Gestational Exposure to Endocrine Disrupting Chemicals Cause Metabolic Dysfunction

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Endocrine disrupting chemicals (EDCs) are ubiquitous in our environment and gestational exposure increases the risk of metabolic diseases in offspring. Humans are exposed to a wide range of EDCs, though much of the research has focused on individual chemicals. Additionally, the mechanism by which gestational exposure adversely affects offspring metabolic health has yet to be elucidated. Extracellular vesicles (EV) have been implicated in the pathogenesis of adult-onset diabetes and are a potential mechanism of mediating fetal programming of diabetes. We hypothesize gestational EDC exposure alters maternal circulating EVs leading to the development of metabolic dysfunction in the offspring. Using a model of EDC exposure, we aimed to elucidate the effect of a physiologically relevant mixture of EDCs on maternal and fetal outcomes. In this model, pregnant Sprague-Dawley rats were exposed in their diet to a mixture of EDCs daily from embryological days 8-18. Dams were evaluated 3 weeks post-delivery at the time of pup weaning and offspring were evaluated at 10-12 weeks of age. We discovered male pups exposed in utero to EDCs were born smaller and caught up to control weight by postnatal day 14. Pancreata from EDC-exposed male offspring had a significant reduction in islet area. Additionally, there was a significant increase in the number of macrophages in the pancreas of EDC-exposed males. In contrast, EDC-exposed females did not differ in body weight, islet size, and macrophage number. Also, the number of maternal circulating EVs was increased, especially those from immune cells. Therefore, we conclude gestational exposure to EDCs results in a sex-specific disruption of pancreatic development and an increase in the maternal biogenesis of circulating EVs. Further research into the role of maternal circulating extracellular vesicles on islet development may identify novel pathways of pathogenesis.

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WS2 Insulin-Induced AKR1C3 Regulates FASN Induction in a Model of Human PCOS Adipocytes

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Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in women of reproductive age. Insulin resistance and hyperandrogenism seen in PCOS could be driving the increased risk for cardio-metabolic comorbidities. Aldo-keto reductase family 1 member C3 (AKR1C3) is induced by insulin in PCOS adipocytes and is the predominant enzyme for the formation of potent androgens, which activate androgen receptor (AR). AR is known to induce fatty acid synthase (FASN), the central enzyme for de novo lipogenesis. Therefore, AR dependent induction of FASN may promote de novo lipogenesis and lipid overload. Activation of this pathway by environmental endocrine disrupting chemicals (EDCs) could drive this increased risk in PCOS women. We hypothesize that insulin signaling induces AKR1C3 to promote lipid overload through FASN in PCOS adipocytes, which could be exacerbated by EDCs. We have previously determined that insulin-induced AKR1C3 increases potent androgen production in human adipocytes and may promote hyperandrogenism in PCOS. Using differentiated human Simpson-Golabi-Behmel Syndrome (SGBS) adipocytes as a model for PCOS adipocytes, we determined that induction of both AKR1C3 and FASN are dependent on PI3K/AKT/mTOR/NRF2 signaling axis using both pharmacological and genetic manipulation. We found that FASN induction is both AKR1C3 and AR dependent, and ARK1C3 stabilizes AR by preventing ubiquitination. We also showed that AKR1C3 and AR interact as seen by co-immunoprecipitation, proximity ligation, and co-occupancy on the FASN locus using ChIP-qPCR assays in a ligand and ligand independent manner. We found that inhibition AKR1C3 and its interaction with AR prevents lipid droplet formation. We conclude that insulin induction of AKR1C3 regulates FASN, which in turn may promote lipid overload in PCOS adipocytes. This work identifies NRF2, AKR1C3, AR, and FASN as possible targets for EDCs to exacerbate cardio-metabolic comorbidities in PCOS women.

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WS3 Mechanism of Perfluorooctanoic Acid Driven Hyperandrogenism in Polycystic Ovary Syndrome

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Polycystic ovary syndrome (PCOS) is the most common endocrinopathy, affecting 8-13% of women during reproductive age. The syndrome is characterized by hyperandrogenism, polycystic ovaries, and failure to ovulate. Current treatment for hyperandrogenism in PCOS patients targets androgen production by the ovaries. However, a large proportion of patients do not see androgen reduction with this treatment, suggesting an alternate source. White adipose tissue (WAT) is an obvious candidate since it produces and secretes hormones. Within WAT, a family of metabolic enzymes, the aldo-keto reductases (AKRs) regulate androgen production. A screen for competitive inhibitors of these enzymes was performed to detect potential endocrine disrupting chemicals in the context of PCOS. Perfluorooctanoic acid (PFOA), a known toxicant, came up as a hit. Interestingly, epidemiological data has observed blood serum samples of patients with PCOS to have higher levels of PFOA compared to non-PCOS individuals. Our data suggests aldo-keto reductase family 1 member C2 (AKR1C2), which predominantly converts the potent androgen dihydrotestosterone to the less potent androgen 3α-androstanediol, to be potently inhibited by PFOA, yielding an observed IC50 value = 205 nM and Ki value = 122 nM. The inhibition was specific for AKR1C2 whereas PFOA did not inhibit the highly related isoforms AKR1C1 and AKR1C3. This inhibition could lead to androgen increase in adipose tissue and potentially contribute to hyperandrogenism in PCOS. The inhibition of AKR1C2 was computationally modeled to detect residue interactions and steric considerations that lead to inhibitor specificity. This modeling is being corroborated by in vitro structure activity relationships with PFOA analogs and site directed mutagenesis. We anticipate that Val 54 in AKR1C2 may be a key component for the specificity since this is the only residue in the steroid binding cavity that is different from the residues in AKR1C1.

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WS4 Investigating the Influence of Periconceptional Exposure to DEHP on DNA Methylation and Disease Risk by Dissecting Windows of DEHP Susceptibility

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Environmental exposure to endocrine disrupting chemicals (EDCs) during fetal and placental development may perturb placental function, a critical determinant of fetal health outcomes throughout pregnancy and post-natal diseases. EDCs in maternal blood can cross into the placenta to disrupt placental growth and vascularization which correlated with low birth weight and increase risk of obesity and diabetes later in life. One EDC strongly associated with these developmental changes is Di-(2-ethylhexyl)-phthalate (DEHP). DEHP is often used in the production of plastics and it is ubiquitous in the environment present in food containers, children's toys, and medical devices. DEHP functions as an anti-androgen in the fetal and placental endocrine systems and interferes with the action of several hormones. As a result, DEHP exposure during pregnancy and/or lactation may result in metabolic and neurological deficits later in life. How these early life challenges elicit lasting effects throughout post-natal life, however, remains unclear. Epigenetic dysregulation has been proposed as a potential mechanism playing a key role in gene-environment interactions. One epigenetic factor, DNA methylation, is particularly vulnerable to environmental exposures as it changes dynamically during fetal development. Offspring phenotypes often depend on the timing of the exposure, thus, we hypothesize that preconception exposure to DEHP alone, similar to a preconception-gestation exposure, disrupts global DNA methylation patterns and growth of the embryo and the placenta. To test this hypothesis, F0 dams were exposed to two doses of DEHP-containing feed (Low: 50 ug/kg/d, High: 10 mg/kg/d) starting two weeks prior to conception until (1) gestational day 0.5 or (2) embryonic day (E) 12.5. We found that High-DEHP exposure during preconception-gestation exposure window causes a reduction in fetal weight and F:P ratio compared to controls. To correlate these findings with molecular changes, our global methylation analysis revealed a significant hypomethylation of E12.5 female placentas exposed to upper-DEHP during preconception and preconception-gestation windows. Finally, we found a reduction in the number of blood vessels on the labyrinth zone of E12.5 placentas using CD34 histological analysis. Our data suggests that DEHP affects fetuses and placentas in a dose- and sex-specific manner..

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EN1 Effects of Bedroom PM2.5, CO2, Temperature, Humidity and Noise on Sleep: an Observational Actigraphy Study

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Objective: The bedroom environment plays a key role for high-quality sleep and sleep hygiene. Studies objectively assessing multiple descriptors of the bedroom environment as well as sleep are scarce.

Methods: PM2.5, temperature, humidity, CO2, barometric pressure and noise levels were measured for 14 consecutive days in the bedroom of 61 participants (62.3% female, mean±SD age 48.0±13.1 years; BMI 30.2±6.5 kg/m2) who wore a wrist actigraph and filled out daily morning surveys and a sleep log.

Results: In a hierarchical mixed effect model adjusted for elapsed sleep time and multiple demographic and behavioral variables, sleep efficiency calculated for consecutive one-hour periods decreased in a dose-dependent manner with increasing levels of PM2.5, temperature, CO2 and noise (all $p<0.02$). Barometric pressure and humidity were not associated with sleep efficiency. Ranked in order of magnitude, sleep efficiency decreased by 2.3%, 2.2%, 1.4%, and 0.3% for each standard deviation increase in PM2.5, noise, temperature and CO2, respectively. Significant interactions between environmental variables suggest synergistic effects of combined exposures on sleep efficiency. No statistically significant effects of the bedroom environment on actigraphically assessed total sleep time or with subjectively assessed sleep onset latency, sleep quality and sleepiness were found. Assessments of bedroom comfort suggest subjective habituation irrespective of exposure levels. Window air conditioning use was associated with lower bedroom temperature (-1.15 ºF, $p=0.0407$) and higher noise levels (+3.84 dBA, $p=0.0209$).

Conclusions: These findings add to a growing body of evidence highlighting the importance of the bedroom environment – beyond the mattress –for high-quality sleep.

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EN2 Identifying Potential ASD-Related Pollutants Through Genetics and Protein-Protein Interactions

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Autism Spectrum Disorders (ASD) are neurodevelopmental disorders characterized by deficits in social communication and stereotyped behavior. While ASD has a strong genetic component, there is increasing evidence of a large role for environmental factors, such as in utero exposures to certain compounds. We hypothesize that investigating molecular pathways for compounds may reveal enrichment of ASD risk genes and therefore provide information on susceptibility to ASD. In this study, we utilized the comparative toxicogenomics database (CTD) for the all known interacting genes/proteins for compounds (interactomes) in conjunction with a list of ASD-associated genes to identify compounds that may affect ASD risk. We identified which compounds had a greater fraction of interaction with ASD genes than expected by chance, thus having a greater associated with ASD. As compound exposure is related to ASD development, deleterious variant burden may provide further evidence to prioritize compounds by identifying which interactomes are most commonly mutated in individuals with ASD compared to controls. To investigate this possibility, we utilized whole genome sequence (WGS) data from the Autism Spectrum Program of Excellence (ASPE). Burden scores for each compound's interactome were calculated by identifying potentially deleterious variants within genes within these interactomes, thereby identifying to which potential compounds ASD individuals may have an increased susceptibility. Interaction networks may provide stronger evidence for relationships between compound interactomes and ASD risk genes at the primary and secondary level, providing key insights into potential targets for further research. To that end, protein-protein interaction (PPI) networks were constructed using the Biological General Repository for Interaction Datasets (BioGRID) and STRING databases. Sub-networks containing interactomes of interest were identified. Mutational burden scores for these sub-networks and enrichment for ASD-risk genes were calculated, to provide further evidence of association with ASD. Our work will provide novel insights into the possible link between ASD-risk genes and susceptibility to compounds which may be strongly associated with ASD. We hope that this integrated approach will provide possible models for more experimental validation of effects of specific compounds on ASD risk.

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CEC1 How Federal and State Regulatory Systems Perpetuate Environmental Injustice in the United States: Industrial Ethylene Oxide Emissions as a Case Study

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Background: Ethylene oxide (EtO), a known human carcinogen, is emitted from facilities across the United States. A 2018 assessment by the Environmental Protection Agency (EPA) showed that areas around EtO-emitting facilities had cancer risk levels up to 24 times the national average. The EPA notified the state Department of Environmental Protection (DEP) about the high cancer risk to their residents. Our aim was to analyze actions and implementation equity at the federal, state, and community levels since the EPA notification.

Methods: Using publicly available data, we identified U.S. emitters of EtO and then analyzed community, state, and federal actions since the EPA notification through content analysis of internet data using the lens of the environmental inequality formation (EIF) theory.

Results: Thirty-one of a total 654 EtO-emitting facilities have an estimated cancer risk of over 100 in a million in neighboring census tracts and are located in 13 states and Puerto Rico, representing 7 EPA regions. Content analysis identified themes of community outcry, agency involvement, and legislative action and found no action without community outcry. By January 2021, 2 facilities had closed, 5 facilities had cut emissions, and 24 facilities in 9 states and 5 EPA regions had taken no action.

Discussion: Wealthier white neighborhoods saw facilities close or cut emissions. Differences in state response correlated with differences in community pressure and state priority setting, resulting in over 1 million people having continued significant EtO exposure for years. Conclusions: The impotence of the federal and state regulatory framework perpetuates environmental injustice in the United States.

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CEC2 Lessons Learned Along the Road to Hazardous Waste Clean-up

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Background: Hazardous Waste clean-up can be contentious. Information gradients and poor communication among stakeholders contribute to confusion, delays, and mistrust. There are very few educational resources for community organizations, governmental agencies and/or commercial entities to improve multi-directional communication while addressing an environmental hazard and navigating the cleanup process. Employing first-hand experiences and lessons learned, we provide a tool for groups beginning the process that supports the evolution of productive relationships between government, regulators and community members.

Methods: In a three-site collaboration among Community Engagement Cores we held a series of discussions distilling unique circumstances and commonalities among sites. We collected media of all types and developed three video modules to help other sites and stakeholders facing the often difficult and lengthy process of achieving hazardous waste clean-up. The "lessons learned" for these modules come from the Fernald OH uranium processing facility site, the Ambler PA asbestos manufacturing site, and the Wilmington MA Olin Chemical Superfund Site, and were developed by a multi-disciplinary team of community stakeholders, professionals in film development and academic partners.

Results: The content addresses: assembling a group including community members, regulators, elected officials and representatives of the commercial site entity; encouraging self-education; conducting an evaluation; productive protesting; speaking with the media; working towards agreement on big concepts; considering cost and feasibility. Samples from the video modules will be shown.

Impact Statement: The well-articulated lessons are presented in an engaging, interactive format and directed towards all stakeholders, providing insights about public health, community planning, and resource development.

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CEC3 Targeted Community Engagement: PES Refinery Exposures

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While in operation, the PES refinery was the largest emitter of volatile organic chemicals in the Philadelphia region. According to the EPA's Toxic Release Inventory, more than four hundred thousand pounds of hazardous chemicals were emitted into the Philadelphia air every year from the PES refinery and more than 10% of the emissions are carcinogens or pre-carcinogens changed into carcinogens in the body. The refinery stood out as the largest emitter impacting the surrounding neighborhoods. The Center of Excellence in Environmental Toxicology has been engaged with the community near the PES refinery through its Community Engagement Core on issues surrounding health effects before and after the shutdown and clean-up of the PES refinery site. The aims of this on-going project are to address community concerns about cancer risk, bring health information to public policymakers, and engage with the community around legacy pollutants and redevelopment. Through this project, the CEET Community Engagement Core has worked with community groups including the United South/Southwest Coalition, the Tasker-Morris Neighborhood Association, and the Eastwick Friends and Neighbors Coalition to ensure meaningful involvement of the community in the redevelopment process at the PES refinery. CEET Researchers have also been involved in this project by analyzing air monitoring data and modeling air flow around the site. We continue to work with community partners, policymakers, and site officials to address the health impacts of legacy pollution and redevelopment plans for the site.

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TBC1 AKR1C3 and DHEA-S in Castration Resistant Prostate Cancer Drug Resistance

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Prostate cancer (PC) is the second most common cancer among American men. PC is fueled by androgen receptor (AR) signaling, where the AR is a nuclear hormone transcription factor that drives growth and proliferation when activated by androgen ligands (ex: Testosterone and DHT). Despite the therapeutic depletion of testosterone used to treat early stage disease, a subset of patients become resistant and develop the lethal form of the disease termed castrate resistant prostate cancer (CRPC) where the disease progresses despite low levels of circulating androgens. CRPC is commonly treated with drugs known as androgen receptor signaling inhibitors (ARSI) that aim to stop this resurgence of AR signaling, however some patients become resistant to these next generation therapeutics and succumb to the disease. A common mode of resistance thought to contribute to this resistance is intratumoral steroidogenesis where androgen precursors from other sources in the body are converted to T and DHT within CRPC cells to activate the AR. ARK1C3 is a steroidogenic enzyme that is involved in every androgen biosynthesis pathway to T and DHT and is also upregulated in CRPC tumors. Here, we demonstrate in a primary tumor PC cell line that a reservoir of DHEA-S from the adrenal gland that remains after ARSI treatment is converted to T in an AKR1C3-dependent manner. Additionally, this reservoir of DHEA-S is sufficient to promote cell growth in an AKR1C3-dependent manner. Taken together, we have identified a mechanism of resistance to ARSI that harnesses AKR1C3 to convert reserves of DHEA-S into cancer-driving steroids.

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