Mini Review

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The CEECHE: a practical approach for reducing exposures and disease outcomes in Central and Eastern Europe

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Abstract: While each region of the world faces unique challenges, environmental threats to vulnerable populations throughout Central and Eastern Europe (CEE) present a significant public health challenge. Environmental pollution is widespread, resulting from the consequences of rapid industrialization during the Soviet Union era. To help address these concerns, a meeting, sponsored in part by the National Institutes of Health (NIH)/National Institute of Environmental Health Sciences (NIEHS) Superfund Research Program (SRP), was convened in 1994. The meeting, “Hazardous Wastes – Exposure, Remediation, and Policy,” brought together representatives of the governments of seven countries in the region, scientists from the United States and Western Europe, and representatives from international organizations to explore hazardous waste problems in the region. Since 1994, the SRP and partners have been holding meetings throughout CEE to share important information regarding environmental health. The general sessions have shifted from a focus on describing the problems in each country related to hazardous waste, exposure assessment, risk reduction, and risk communication, to an exchange of information to better define links between health and the environment and strategies to improve regional problems. The 1994 meeting and subsequent meetings raised issues such as heavy metal contamination, exposures from hazardous waste, and pollution caused by deficiencies in disposal of waste overall. Research priorities that were identified included development of reliable biomarkers, better understanding of the relationship between nutrition and chemical toxicity, more epidemiological studies in CEE, better methods of environmental data analysis, and development of remediation tools. Here, we review examples of research from current SRP grantees that address many of these issues. In 2004, the first official Central and Eastern European Conference on Health and the Environment (CEECHE) was held, and has been held biannually at venues across CEE. The CEECHE provides a forum for researchers and engineers, and organizations with diverse professional expertise and backgrounds, to jointly examine pressing environment and health issues, engage in cooperative research, and develop and disseminate innovative prevention strategies for addressing these issues. The CEECHE facilitates more intentional integration of disciplines to achieve a fundamental understanding of biological, environmental, and engineering processes and exploit this knowledge to contribute to solving environmental exposure-related issues. Critical to the CEECHE mission is the participation of trainees and junior scientists who will share their data and engage broadly with the scientific community. Scientific inquiry that supports a paradigm whereby knowledge gained through understanding disease processes resulting from environmental exposures would further our understanding of potential human health effects, and provide a creative, holistic approach to integrate seemingly discrete biological systems and ecological and human health risk assessments into more comprehensive models. Such models will be discussed which advance the mission of reducing the public health burden of hazardous substances through interdisciplinary research and training.

Keywords: environmental health; global health; hazardous waste; networks; policy; remediation.

Introduction

Central and Eastern Europe (CEE) faces its own unique environmental health challenges, as does every region of the world. In CEE, environmental threats to vulnerable populations are significant, much of it the result of quick industrialization that happened during the tenure of the Soviet Union, with no industrial, occupational, or environmental controls put into place. A high-profile outcome of those conditions was the Chernobyl disaster in 1986. This

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era of industrialization was followed by the disintegration of industries with the fall of the Soviet Union in 1991 (1).

One major health threat that has resulted is uranium contamination. The Soviet Union mined uranium for decades, leaving mines in CEE (2). The Czech Republic and Romania have no national strategy for monitoring the health of former miners or locals who live near former mines. The cancer risk from radiation has not been sufficiently analyzed in the region, so deaths caused by cancer stemming from uranium mining are unknown (2). According to Romania’s ministry of health, the main route of radioactive exposure for uranium miners is via inhaling radon (2).

Waste disposal in general also presents a problem for the region. Despite blanket waste targets in Europe, many countries in CEE break European laws without obvious consequence. For example, Bulgaria, the Czech Republic, Poland, Romania, Slovakia, and Slovenia missed the 2010 and 2013 targets for diverting biodegradable municipal waste from landfills (3). In addition, major differences exist in waste treatment throughout Europe. For example, in 2013, Denmark created more waste per capita than Romania, but sent much less of it to the landfill (3).

The beginnings of an organized network

In the last 20 years, environmental scientists and engineers in the CEE region began organizing themselves to address these problems through a series of scientific meetings. Over the years, staff and grantees of the National Institutes of Health (NIH)/National Institute of Environmental Health Sciences (NIEHS) Superfund Research Program (SRP) have participated in a number of these conferences in CEE as invited speakers, keynote speakers, or conference co-chairs and co-organizers. These meetings have helped transfer knowledge between the United States and CEE and have encouraged interdisciplinary and international collaboration on risk assessment, environmental decision-making, remediation, and environmental health.

The first meeting was held in Prague in 1994. The 1994 Prague meeting brought together 13 countries and addressed various research needs surrounding hazardous wastes, including exposure, remediation, and policy. Present were representatives from seven CEE countries and scientists from the United States and Western Europe. These participants focused on describing the problems in each country related to hazardous waste.

The 1994 meeting and other early meetings identified general problems in the region of heavy metals, persistent organics, hospital waste, air pollution, and ionizing radiation. The identified research priorities included the need for reliable biomarkers, better understanding of the relationship between nutrition and chemical toxicity, more epidemiological studies in CEE, better methods of environmental data analysis, and development of remediation tools.

The following year, a second conference was held in Prague on environmental mutagens in human populations. In 1996, a meeting in Sosnowiec addressed environmental pollution and children’s health, two critical issues for the region. Main topics of discussion were lead exposure assessment and health effects, air pollution, congenital malformations, and ionizing radiation. Also discussed were methods to measure reproductive outcomes, using birth registries, and biomonitoring. A subsequent meeting in 1998 tackled remediation of hazardous wastes, technology, and health effects.

Over the years, the general sessions have shifted from a focus on describing the problems in each country related to hazardous waste, exposure assessment, risk reduction, and risk communication, to an exchange of information to better define links between health and the environment and strategies to improve regional problems. In 2000, the United States/Central Europe meeting focused on metals in the region, a recurring theme. These discussions included sources of contamination and methods of remediation. Researchers shared knowledge about identifying markers of exposure, risk assessment, and communication management, assessing health effects (including neurodevelopmental effects in children), measuring uptake in plants and food webs, and remediation in soil.

It was not until a decade after that first meeting in Prague that these periodic meetings resulted in the formation of an official organization – the Central and Eastern European Conference on Health and the Environment (CEECHE). In 2004, the first official meeting of the CEECHE was held in Prague. Scientists continued discussion of the broad themes of hazardous waste exposure, children’s health, and remediation.

The 2004 meeting also focused specifically on trainees, who were given an opportunity to share research and engage with the scientific community. Panel discussions were held for students and young investigators. This activity led to the publication of a commentary authored by young investigators from nine different countries that identified environmental health concerns in CEE, offered potential solutions, and emphasized the importance of exchange of information between developed and developing countries (4). Such activities have given a voice to trainees from CEE, where the trainee-professor relationship historically has had more of a hierarchical structure.
than in Western countries. The inclusion of trainees from CEE at these meetings has exposed them to the type of open dialogue between trainees and their mentors that is common in Western states.

As of the most recent CEECHE meeting in 2016, the SRP and scientists from CEE have been exchanging ideas and information about environmental health for more than 20 years. The variety of sessions in 2016 exemplify how SRP grantees and our European collaborators continue to address the needs identified at early meetings in CEE (see Table 1). The sessions focus on a variety of topics related to human health and the environment including how to address complex exposures, how to better understand population health impacts, innovative detection and remediation technologies, preventing multi-level disease through multi-level interventions, addressing policies associated with prevention, as well as other special topics.

### Changing exposures in a changing world

Though progress has been made, new challenges globally are putting pressure on CEE and the world. The location, intensity, and frequency of environmental exposures are changing rapidly. Specific challenges include rapid globalization, new industrialization, pervasive poverty and inequity (5), non-sustainable consumption, excessive population growth, and movement of chemicals across national and international boundaries.

Contamination with heavy metals such as lead was a significant issue for the CEE region in the very first meeting in which SRP was involved in, in 1994, and metals still pose a substantial environmental health threat in the region today. New sources of metal contamination include exposures from recycling of electronic waste, or e-waste. Household electric and electronic equipment in Romania in 2015 was significant: it amounted to 7.3 kg/person (6). Only 30% was recovered and treated in authorized scrap collection plants. Much of the e-waste generated is collected by informal “street scrap pickers” who immediately remove the valuable parts, leaving the other untreated components behind (6).

Unfortunately, informal electronics recycling in developing countries is primitive and is carried out by migrant workers who are poor and not concerned for their health. They are just trying to feed their families. Examples of tasks performed by these workers include burning wires to harvest copper, which has the

### Table 1: How is CEECHE addressing identified research needs?

<table>
<thead>
<tr>
<th>Identified need</th>
<th>Investigator</th>
<th>Description of project</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reliable biomarkers</td>
<td>Michael Petriello, University of Kentucky</td>
<td>Plasma levels of the pro-atherogenic biomarker TMAO as a biomarker for dioxin-like pollutants</td>
</tr>
<tr>
<td>Reliable biomarkers</td>
<td>Pavel Babica, Masaryk University in the Czech Republic</td>
<td>Gap junctional intercellular communication is a biomarker for assessing environmental stressors and chemopreventive compounds</td>
</tr>
<tr>
<td>Nutrition and chemical toxicity</td>
<td>Andrew Hennig, University of Kentucky</td>
<td>Nutritional modulation of the toxicity of environmental pollutants and its implications in public health</td>
</tr>
<tr>
<td>Nutrition and chemical toxicity</td>
<td>Andrew Morris, University of Kentucky</td>
<td>Mechanisms linking diet and environmental pollutant-associated diabetes and cardiovascular disease risk</td>
</tr>
<tr>
<td>Epidemiological studies in CEE</td>
<td>Ondřej Mikeš, Masaryk University, Czech Republic</td>
<td>Relationship between dietary patterns in pregnancy and birth outcomes in an ELSPAC longitudinal study</td>
</tr>
<tr>
<td>Epidemiological studies in CEE</td>
<td>Miroslav Dostál, Institute of Experimental Medicine AS CR, Czech Republic</td>
<td>Evidence on effects of ultrafine particles on the respiratory health of children – results from the UFIREG study</td>
</tr>
<tr>
<td>Environmental data analysis</td>
<td>Eric Suubert, Brown University</td>
<td>Vapor intrusion and the use of mathematical models to predict transients in exposures</td>
</tr>
<tr>
<td>Environmental data analysis</td>
<td>Anna Palday, National Public Health Center, Hungary</td>
<td>The study of heat-wave-related excess mortality in Hungary at a small area (NUTS4) level, 2005–2014</td>
</tr>
<tr>
<td>Remediation tools</td>
<td>Stanisław Gawronski, Warsaw University of Life Sciences, Poland</td>
<td>Indoor air quality improvement by the use of environmental biotechnology – phytoremediation</td>
</tr>
<tr>
<td>Remediation tools</td>
<td>Ondrej Uhlik, University of Chemistry and Technology, Prague, Czech Republic</td>
<td>Assessing the bioremediation potential of indigenous microbial communities in contaminated matrices</td>
</tr>
</tbody>
</table>

At the 2016 meeting of the CEECHE, several collaborators from the United States and the CEE region presented examples of research that is addressing needs that were identified at earlier meetings of the organization.
unintended consequence of releasing harmful dioxins and furans into the air. Polycyclic aromatic hydrocarbons (PAHs) are also released into the air. Other routes of exposure include dust from burn sites accumulating on food, and hazardous substances in the soil seeping into nearby water supplies (7, 8).

Another large health threat worldwide is the plethora of synthetic chemicals that are being introduced into the marketplace for use in household products and as pharmaceuticals. Thousands of new synthetic chemicals are introduced into the international marketplace each year (9). This pace of production has continued since World War II (9).

All of these developments are happening in a time of uncertainty brought about by predicted global environmental change, which will increase the propensity for natural disasters.

The need to integrate and share data

The adverse health consequences of exposure to environmental toxicants constitute a large and rapidly growing global problem, yet they receive insufficient attention in the global health and international development agendas (10). According to the World Health Organization (WHO), 23% of all global deaths are linked to the environment. That is approximately 12.6 million deaths per year (11). Cancer, for instance, is a disease with a strong environmental component. It poses a major threat to public health worldwide, and incidence rates have increased in most countries since 1990. In men, mortality rates from cancer are higher in CEE than in any other region in the world (173 per 100,000) (12).

To address such problems, scientists are increasingly embracing the idea that it is important to measure the “exposome” – the totality of exposure an individual is subjected to from conception to death (13, 14). To fully understand the risk of disease, we must measure as many human exposures and responses we can, across multiple time points. This type of “unbiased” exposure measurement is very data driven.

Because exposure and response data is growing evermore complex, a challenge in reducing environmental health threats is the need to integrate and share diverse data formats from a variety of scientists – from engineers to microbiologists. To enhance the knowledge based to reduce the burden of disease and improve public health will require:

- Coordinated data collection on environmental exposures related to health effects and disease etiologies
- A global, strategic epidemiological effort on the relationship between environmental exposure and ill health
- Intervention designs that consider the entire environmental exposure pathway from driving forces to health impact
- Prevention methods backed by research on mechanism(s) and interactions between infectious diseases, environmental exposures, and genetics.

Looking to the future of the CEECHE

As environmental threats in the CEE region are becoming more complex, the importance of networks such as CEECHE has only grown. Several other organizations serve as models for creating global networks that the CEECHE would do well to emulate as it evolves. One is the SRP, which, at its heart, is a network designed to create solutions to complex problems. The second is the WHO collaborating centres – an information-sharing network. The third is a proposed global infrastructure to drive the development of technologies.

The Superfund Research Program

The SRP is a model from the research standpoint, and the CEECHE has been closely linked to the SRP since its inception. Supported by the NIEHS, the SRP funds research related to remediation approaches, detection technologies, fate and transport modeling, bioavailability and ecotoxicity, and ecological and human risk assessments. The SRP is an international network that fosters collaboration among basic, clinical, behavioral scientists, and engineers. At its core is a coordinated program of research and prevention centers that conduct research to understand and address the environmental aspects of disease. The centers’ activities include exposure assessment, health effects research, development and validation of strategies for risk management and disease prevention, and development of engineering strategies to reduce risk. The individual centers are housed jointly within schools of public health and engineering. An important part of SRP-funded centers is engagement with the communities affected by hazardous waste. The basic premise of all the centers is that hazardous waste is a complex problem; we know that hazardous substances are migrating into soil,
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The World Health Organization collaborating centers

The WHO collaborating centers serve as a model from a coordinated data collection standpoint. The network comprises 10 research institutes around the world, each acting as a hub to strengthen national or regional capacity to advance children’s environmental health. At the same time, collaboration and the sharing of services and expertise among centers in the network builds global capacity in children’s environmental health. Much like the CEECHE, the WHO centers, which were established in 2014, are the result of a formalized network among those that had worked together informally in the past. The centers participate in quarterly conference calls and collaborate on publications. New websites for participating centers are continually updated and highlight research interests and available cohorts. Future plans include holding satellite meetings when members of the centers are together at other meetings, and beginning to widen the network to include non-governmental organizations that work on children’s environmental health in low- and middle-income countries, as well as the NIEHS-Environmental Protection Agency’s Children’s Environmental Health and Disease Prevention Centers.

The Global Human Health Sciences and Technology Initiative

Finally, there is a need for a Global Human Health Sciences and Technology Initiative – a virtual infrastructure that houses a team of scientists and engineers who conduct research in the emerging area of exposure biology framed on emerging global health issues. One focus for the organization will be the development of technologies to accurately predict human biological response to exposure induced by external agents. These improved biomarkers will eventually translate to more accurate, faster, and less expensive clinical trials. A second activity will be disease intervention, focused on a broad, informatics-based program, aimed at identification of chemical agents that result in reduction in disease burden. Detailed knowledge of disease-specific biochemical networks will be used to design agents that attack multiple nodes in the biochemical networks of diseased cells. Finally, the initiative will build upon existing, modest-scope epidemiological studies by adding to them a host of modern measurement tools that, in aggregate, will provide the most detailed phenotypic definition of a population in any epidemiologic study done to date. This model should allow better prediction of disease risk and should provide better access to customized medical care. This initiative will build upon current advancements in data science and analytics.

As the CEECHE grows and evolves, its network of collaborators will complement these and other networks that are aiming to reduce the health burden from hazardous substances through interdisciplinary research and training. Such networks are vital for developing better methods to prevent environmentally mediated disease (15). Moving forward, the CEECHE could benefit from a more robust administrative management structure to ensure the continued activity of the CEECHE meeting, the organization, and the fruitful research collaborations it has spawned. For instance, a similar organization focused on environmental health problems in the Pacific Basin region holds regular meetings every two years, has created formal bylaws, and has appointed an executive officer (16). All of these networks bring together investigators from the biomedical sciences and the non-biomedical sciences, such as engineering, who would not normally collaborate in a single scientific meeting to address specific complex problems. It is only through such transdisciplinary work that we can solve the complex environmental health threats that face us today.

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