

Columbia University 2014 SRP Annual Updates

A. Overall Center Highlights

In this section we highlight what we consider to be some of the major accomplishments during the past grant period. Progress reports for each of the individual projects and cores provide more detailed information about specific achievements related to each specific aim.

1. Major Activities: We are particularly proud of a major activity carried out by Community Engagement PI Yan Zheng and USGS Hydrologist Joseph Ayotte. Together they have focused on the problem of arsenic contamination of drinking water in the United States, and have edited a special issue on arsenic for the journal *Science of the Total Environment (STOTEN)* that will be published on February 1, 2015. Their summary paper, *“At the crossroads: Hazard assessment and reduction of health risks from arsenic in private well waters of the northeastern United States and Atlantic Canada”* will be the first in a collection of **thirteen papers** that provides state-of-the-art information on arsenic hydrogeochemistry, effectiveness of household well treatment systems, and the testing and treatment decisions of private well owners in several northeastern U.S. states and in Nova Scotia, Canada. Six additional papers in the STOTEN special issue are also co-authored by Columbia SRP scientists and their partners. Zheng and Ayotte conclude in their summary that there must be an overall, long-term strategy to reduce exposure to vulnerable populations in regions where levels of arsenic in well-water are high. More consideration is needed to encourage well testing, treatment, access to alternative water sources, and possible implementation of local, state, and regional private well-water regulations.

2. Significant Results Concerning Arsenic Metabolism: Inorganic arsenic(As) is metabolized through a series of methylation reactions catalyzed by arsenic(III)-methyltransferase (AS3MT), resulting in the generation of monomethylarsonic (MMAs) and dimethylarsinic acids (DMAs). AS3MT activity requires the presence of the methyl donor S-adenosylmethionine, a product of folate-dependent one-carbon metabolism, and a reductant. Although glutathione (GSH), the primary endogenous antioxidant, is not required for As methylation, GSH stimulates As methylation rates in vitro. However, the relationship between GSH redox and As methylation capacity in humans is unknown. SRP trainee, Megan Niedzwiecki, wished to test the hypothesis that a more oxidized plasma GSH redox status is associated with decreased As methylation capacity and to examine whether these associations are modified by folate nutritional status. Concentrations of plasma GSH and GSSG, plasma folate, total blood As (bAs), total urinary As (uAs), and uAs metabolites were assessed in a cross-sectional study of Bangladeshi adults who were chronically exposed to As in drinking water. We observed that a decreased plasma GSH/GSSG ratio (reflecting a more oxidized redox state) was significantly associated with increased urinary %MMA, decreased urinary %DMA, and increased total bAs in folate-deficient individuals (plasma folate ≤ 9.0 nmol/L). Concentrations of plasma GSH and GSSG were independently associated with increased and decreased As methylation capacity, respectively. No significant associations were observed in folate-sufficient individuals, and interactions by folate status were statistically significant. Our findings, published in *Free Radical Biology & Medicine* in 2014, suggest that GSH/GSSG redox regulation might contribute to the large interindividual variation in As methylation capacity observed in human populations. This is important because arsenic methylation, which influences its toxicity, is potentially modifiable in human populations.

3. Significant Results Concerning Enhanced Mitigation Methods for Arsenic at US Superfund Sites: Magnetite is stable across typical groundwater redox conditions and important for arsenic sorption, and therefore may represent a long-term host-mineral for arsenic. Previous laboratory column experiments, which used aquifer sediment from Dover Municipal Landfill Site, produced magnetite and Fe(III) oxyhydroxides through the oxidation of ferrous iron by nitrate. This mineral assemblage effectively removed arsenic from solution even under prolonged reduction and continued to sequester arsenic for an extended period of time. A satisfactory identification of the geochemical and hydrological processes critical for arsenic sequestration and a good understanding of how these processes differ at field-scale, are needed to develop field strategies. An initial reactive transport model was designed for the columns, which provided a detailed description and quantification of the processes affecting the changes observed in the laboratory columns. The model was then combined with the existing site's flow model to predict the spatial and temporal evolution of these critical processes during field trials. The model will serve as a foundation to help evaluate the evolution of the magnetite based strategy in field systems and achieve successful remediation. These findings are significant because current immobilization strategies for arsenic contaminated sites are often ineffective, in part because iron host minerals are often unstable under redox changes. The Columbia SRP has demonstrated that magnetite can potentially serve as a stable host-mineral for long-term arsenic immobilization and are working on the strategy of *in situ* porous reactive filters of magnetite. Numerical modeling has allowed parameterization of the data gleaned from laboratory experiments and is helping to design field-deployable procedures.

4. Other Achievements: Since some of our research involves adults and children exposed to arsenic in Bangladesh, we have always had an emphasis on discovering new measures by which arsenic exposure can be reduced in these study populations, whether by technological or social/educational means. We are therefore proud of our finding regarding the evaluation of an elementary school-based intervention for reducing arsenic exposure in Bangladesh, conducted by Bangladeshi-American PhD student (now graduate) Khalid Khan, whose work is about to be published in EHP. In short, we recruited 840 children from 14 elementary schools in Araihasar, Bangladesh. Teachers from 7 of these schools, randomly selected by cluster sampling, were trained on an As education curriculum, which they implemented by explaining the risks of As exposure over an 18-month intervention period. The remaining seven schools without any such program formed the control group. Surveys, knowledge tests and well-water testing were conducted on all children both at baseline and post-intervention follow-up. Half of the children from each group provided urine samples. The presence of one low As community well in each study village was ensured during intervention. After adjustment for the number of low As wells within 200 meters from homes and other socio-demographic confounders, children receiving the intervention were five times more likely to switch from high to low As wells ($p < 0.001$). Consistent with this finding, we also observed a significant decline of urinary As ($p = < 0.001$) (estimated $\beta = -214.9$; 95% CI: $-301.1, -128.7$) and significantly improved As knowledge attributable to the intervention after controlling for potential confounding variables. ***These findings offer strong evidence of the efficacy of school-based educational intervention that has remarkable potential to motivate teachers, children and parents of the students at the same time.***

Highlight - Project #2: “Evaluation of an elementary school-based intervention for reducing arsenic exposure in Bangladesh.”

Objectives: Chronic exposure to arsenic (As) from drinking tubewell water remains a major rural health challenge in Bangladesh and many other developing countries. This study quantifies the extent to which school-based education can enhance the impact of As mitigation.

Methods: We recruited 840 children from 14 elementary schools in Araihasar, Bangladesh. Teachers from 7 of these schools, randomly selected by cluster sampling, were trained on an As education curriculum, which they implemented by explaining the risks of As exposure over an 18-month intervention period. The remaining seven schools without any such program formed the control group. Surveys, knowledge tests and well-water testing were conducted on all children both at baseline and post-intervention follow-up. Half of the children from each group provided urine samples. The presence of one low As community well in each study village was ensured during intervention.

Results: After adjustment for the number of low As wells within 200 meters from homes and other socio-demographic confounders, children receiving the intervention were five times more likely to switch from high to low As wells ($p < 0.001$). Consistent with this finding, we also observed a significant decline of urinary As ($p < 0.001$) (estimated $\beta = -214.9$; 95% CI: -301.1, -128.7) and significantly improved As knowledge attributable to the intervention after controlling for potential confounding variables.

Significance: These findings offer strong evidence of the efficacy of school-based educational intervention that has remarkable potential to motivate teachers, children and parents of the students at the same time.

Khan K, Ahmed E, Factor-Litvak P,¹ Liu X,¹ Siddique AB, Wasserman GA, Slavkovich V, Levy D, Mey JL, van Geen A, Graziano JH. Evaluation of an Elementary School-based Educational Intervention for Reducing Arsenic Exposure in Bangladesh. Under review of minor revisions, Environ Health Perspect, Jan 2015.

Highlight - Project 6: Defining the Sustainable Uses of Low-Arsenic Aquifers in Bangladesh Increasing the impact of deep-well installations to reduce arsenic exposure in Bangladesh.

Our recent field survey of tubewells conducted in a representative area of Bangladesh showed that 54% of the (mostly shallow) tubewells met the Bangladesh standard of 50 $\mu\text{g/L}$ for arsenic in drinking water but a majority of well owners (63%) did not know the status of their well. However, 92% of the 916 intermediate (90-150 m) and deep (>150 m) wells installed by the government and donors met the World Health Organization guideline for As in drinking water of 10 $\mu\text{g/L}$. Only 9 of the deep wells did not meet the Bangladesh standard of 50 $\mu\text{g/L}$; 5 of these had leaky casings allowing high-As water to enter. These findings confirm that deep community wells are crucial for reducing exposure to arsenic in many parts of rural Bangladesh. The choice of sites where deep wells are installed in the future clearly needs to be rationalized, however. Only 29% of the 22,280 high-As wells in the area are located within walking distance (100 m) of the 916 intermediate and deep wells; 74% could have been if the same number of deep wells had been more evenly distributed instead of being clustered in a subset of villages. In order to increase their impact, intermediate and deep wells tapping low As aquifers throughout Bangladesh should be installed at least 200 m apart in publicly accessible areas.

Significance: Although the government branch responsible for allocating deep wells in Bangladesh, the Department of Public Health Engineering, had anecdotal evidence that subsidies were high-jacked by wealthy or politically-connected households to install a deep well on their own property, they were reportedly shocked by the scale of the problem based on our findings. Policy remediation is now actively being considered.

van Geen A, KM Ahmed, EB Ahmed, I Choudhury, MR Mozumder, BC Bostick, BJ Mailloux. Increasing the impact of deep-well installations to reduce arsenic exposure in Bangladesh. Submitted to Environmental Science and Technology, November 2014.

Highlight - Community Engagement Core

PI Yan Zheng and USGS Hydrologist Joseph Ayotte together have edited a special issue on arsenic for the journal *Science of the Total Environment (STOTEN)* that will be published on February 1, 2015. Their summary paper, "At the crossroads: Hazard assessment and reduction of health risks from arsenic in private well waters of the northeastern United States and Atlantic Canada" will be the first in a collection of thirteen papers that provides state-of-the-art information on arsenic (As) hydrogeochemistry, effectiveness of household well treatment systems, and the testing and treatment decisions of private well owners in several northeastern U.S. states and in Nova Scotia, Canada. Six additional papers in the STOTEN special issue are also co-authored by Columbia SRP scientists and their partners. Zheng and Ayotte conclude in their summary that there must be an overall, long-term strategy to reduce exposure to vulnerable populations in regions where levels of arsenic in well-water are high. More consideration is needed to encourage well testing, treatment, access to alternative water sources, and possible implementation of local, state, and regional private well-water regulations.

Zheng, Yan and Joseph D. Ayotte. (2015) At the crossroads: Hazard assessment and reduction of health risks from arsenic in private well waters of the northeastern United States and Atlantic Canada. *Science of The Total Environment, Volume 505, Pages 1237-1247*. Available online 18 November 2014, doi:10.1016/j.scitotenv.2014.10.089. PMID: 25466685, PMCID: in process

B. Trainee Highlights

While the Columbia University SRP does not contain a Training Core per se, it has provided numerous training opportunities for both pre- and post-doctoral trainees. Six PhD students and two post-doctoral fellows have been engaged in the six research projects funded by this SRP grant during the past year. Collectively these students have made research presentations at a number of national and international research conferences including: the annual SRP meeting, Society of Toxicology meeting, the FASEB summer research conference on folate and one carbon metabolism, the Geological Society of American, the American Society of Agronomy, the Crop Science Society of America, and the Soil Science Society of America.

Each of the PhD students has taken graduate course work that is required by their respective departments, i.e., the Department of Environmental Health Sciences at the Mailman School of Public

Health, and the Department of Earth and Environmental Science at the Lamont Doherty Earth Observatory. One student has recently graduated (Megan Niedzwicki) and is now a post-doctoral fellow at the Mount Sinai School of Medicine. A second (Brandilyn Peters) is about to defend her dissertation and has accepted a post-doctoral position at New York University.

All of our students and post-doctoral fellows are active participants in the SRP's monthly seminar program, which has been described at length in the progress report of the Administrative Core. In addition, all are engaged in weekly laboratory meetings of their respective PIs, which include Drs. Ahsan, Graziano, van Geen, Chillrud, Bostick and Gamble.

Trainee Success Story: Former trainee Khalid Khan is now an Assistant Professor of Environmental Health at the School of Public Health at Indiana University. Khalid's field research and stipend was supported by a Fogarty ITREOH grant, but his laboratory work was supported by the Trace Elements Core and Biogeochemistry Cores of our SRP grant. Khalid received his DrPH degree from Columbia University in 2010 and was Dr. Graziano's student. His work sought to reduce environmental arsenic exposure in children in Bangladesh. One of his final publications from his dissertation work at Columbia University, arguably his most important work is about to be published in *Environmental Health Perspectives*, entitled "Evaluation of an elementary school-based intervention for reducing arsenic exposure in Bangladesh." In his study of 840 children across 14 elementary schools in Araihaazar, Bangladesh, his findings offer strong evidence of the efficacy of school-based educational intervention that has remarkable potential to motivate teachers, children and parents of the students at the same time. EHP required minor revisions to the manuscript, and these were submitted on January 16, 2015. We expect the paper to be available on-line at EHP imminently.

Current Trainees: **Tiffany Sanchez** is the only current PhD student trainee involved with Project #2. The evaluation of the relationship between As exposure and non-malignant respiratory disease will comprise the basis of Tiffany's PhD dissertation. We anticipate that she will defend her dissertation in May, 2016.

In early 2014, Tiffany traveled to Bangladesh to monitor the study. She met with field staff, visited study participants and transported biological samples to New York for analyses. Upon her return, she worked in Dr. Matthew Perzanowski's laboratory analyzing pH in Exhaled Breath Condensate (EBC) samples. She will next work with Dr. Beizhan Yan learning a LC-MS/MS technique to analyze 8-isoprostane in EBC. Outside of the lab, Tiffany presented a poster at the Superfund Research Program's annual meeting in San Jose, CA, entitled "Limited impact of point-of-use filters on arsenic exposure in the Folate and Creatinine Trial (FACT)." Tiffany is also about to start an interim analyses of pulmonary function tests for the study. She intends to present her findings at the International Society for Environmental Epidemiology's annual conference later this year.

C. Research Translation and Community Engagement Highlights

Three significant highlights of dissemination to communities of interest, derived from our Research Translation and Community Engagement Cores are provided below:

Highlight #1: CU SRP Director Joseph Graziano for the past 2 years has led the National Research Council (NRC) committee to evaluate critical scientific issues to assess cancer and non-cancer effects from oral exposure to inorganic arsenic. In 2014 the NRC committee released its Interim Report on “Critical Aspects of EPA’s IRIS Assessment of Inorganic Arsenic”. This report is the culmination of workshops led by Graziano to gather and evaluate a variety of expertise and perspectives from arsenic researchers (including SRP PIs Mary Gamble and Clark Lantz), risk-assessment professionals, key stakeholders, and the public. The Interim Report addresses the NRC project’s first phase by providing recommendations on key aspects and controversies related to the performance of inorganic arsenic hazard identification and dose–response analyses and on how EPA’s IRIS assessment should address these issues. Once EPA revises the IRIS assessment, Graziano with the committee will review it to determine whether the scientific was adequately evaluated, whether appropriate methods were used to derive cancer risk estimates and noncancer reference values, and whether dose-response relationships between inorganic arsenic and cancer/noncancer effects were appropriately estimated and characterized. The NRC convened the committee at the request of EPA in response to a congressional mandate for an independent review of the Integrated Risk Information System (IRIS) assessment of inorganic arsenic. Committee members also include CU SRP Principal Investigator Habibul Ahsan and as well as SRP grantees Margaret Karagas, Rebecca Fry, and Robert Wright.

Highlight #2: Community Engagement PI Yan Zheng and USGS Hydrologist Joseph Ayotte together have edited a special issue on arsenic for the journal *Science of the Total Environment (STOTEN)* that will be published on February 1, 2015. Their summary paper, “At the crossroads: Hazard assessment and reduction of health risks from arsenic in private well waters of the northeastern United States and Atlantic Canada” will be the first in a collection of thirteen papers that provides state-of-the-art information on arsenic (As) hydrogeochemistry, effectiveness of household well treatment systems, and the testing and treatment decisions of private well owners in several northeastern U.S. states and in Nova Scotia, Canada. Six additional papers in the STOTEN special issue are also co-authored by Columbia SRP scientists and their partners. Zheng and Ayotte conclude in their summary that there must be an overall, long-term strategy to reduce exposure to vulnerable populations in regions where levels of arsenic in well-water are high. More consideration is needed to encourage well testing, treatment, access to alternative water sources, and possible implementation of local, state, and regional private well-water regulations.

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Highlight #3: The fourth Research Translation Core video project, part of the CU SRP series of awareness/educational videos aimed at private well owners in areas with high arsenic, was initiated by the fall 2014 Barnard Sustainable Development Workshop. This video focuses on well owners who have made the decision to treat their water for arsenic and now need to make an informed decision about which treatment system to purchase. As with the previous videos the student workshops work as a consulting team for a non-academic client, in this case, the NJDEP individual at the center of the state’s response to arsenic contamination. To support both the video development and NJDEP public information efforts a survey of arsenic treatment providers in NJ was undertaken. The initial draft of the video has been completed and will be revised and completed following a Q1 review process.

D. Project/Core Progress Updates

Project 1. A Cohort Study of Health Effects of Arsenic Exposure in Bangladesh: PI-Habib Ahsan

This prospective cohort named as “Health Effects of Arsenic Longitudinal Study” was established in the first Superfund funding cycle by recruiting 11,746 men and women in Araidhazar, Bangladesh, during 2000-2002 to investigate the health effects of arsenic exposure, with an initial focus on skin lesions and skin cancers. The design of this multidisciplinary project and cohort description has been published (Ahsan et al., 2005). Over the successive funding cycles, the cohort was expanded through both Superfund as well as other funding and the number of cohort members currently stands at 35,046. In addition to extensive questionnaire data, blood and urine samples are collected from all cohort members at recruitment. Each cohort member gets followed-up through in-person interviews on average every three years. A sample of urine is collected during the follow-up visits. Data on major diseases and mortality (including their causes) are ascertained as part of the follow-up process. Given the multiple phases of expansion of the cohort, the cohort members recruited earlier years have accrued longer follow-up than the recently recruited members. Most of our ongoing and recently-completed analyses involve prospective data on 20,000 cohort members recruited as of 2011. The latest follow-up cycle, which has just begun, includes a unified approach to follow all 35,046 cohort members using a single data collection instrument in one-go. This synching of data collection for all cohort members will allow us analyzing follow-up data of all 35,046 cohort members recruited to date in analyses after this follow-up cycle is completed. To date, we have numerous publications utilizing the baseline cross-sectional data on arsenic exposure and adverse health effects, including prevalent skin lesion cases, as well as longitudinal analyses of mortality, incident skin lesions, diabetes, cardiovascular disease, and respiratory disease with the prospective data.

Project 2. Consequences of Arsenic and Manganese Exposure on Children: PI-Joseph Graziano

The goal of Project 2 is to address several questions concerning the health effects of exposure to arsenic and manganese in water (WAs and WMn, respectively) among adolescents. First, does the As-induced respiratory disease observed in adults also manifest itself in adolescents, and what are possible physiologic mechanisms? Second, to what extent do associations between WAs and both lung function brain function reflect the effects of exposure in utero and in infancy, periods of dramatic development for these systems? Third, are WAs and WMn associated with specific cognitive functions in addition to intelligence? We will draw on an existing sample of 780 adolescents (15-17 years old) whose mothers are participants in the HEALS cohort study (Project #1). Based on mothers' well As, measured five times from 2000 until the present, we are able to define four groups of adolescents with varying levels and patterns of exposure to As. Defined on the basis of WAs levels, four groups include adolescents with exposures that are: Group 1) consistently low (mean WAs = 3 ppb); Group 2) consistently moderate (mean WAs = 26 ppb); Group 3) consistently high (mean WAs = 146 ppb); and Group 4) high from conception through roughly age one (mean WAs = 201 ppb) but much lower thereafter (mean WAs = 13 ppb). Within each group, there is wide variation in WMn concentrations. Three specific aims target As exposure and pulmonary function (FEV1 and FVC) as well as biomarkers of lung dysfunction in exhaled breath condensate. An additional three aims focus on neuropsychologic outcomes by considering components of Executive Function (planning, sustained attention, working memory) that have been mapped to brain regions thought to be affected by exposure to these elements. Components of Executive Function will be measured with the Cambridge Neuropsychological Test Automated Battery

(CANTAB), a computerized and well validated set of tests; intelligence will also be assessed. To date, recruitment and field work have gone very well and we anticipate that all of the field work will be completed by the fall of 2015. Interim analyses of several of the specific aims are in progress.

Project 3. Impact of Nutrition on Arsenic-Induced Epigenetic Dysregulation: PI-Mary Gamble

The carcinogenic and non-carcinogenic mechanisms of As are incompletely understood, but an emerging body of evidence suggests that As exposure leads to dysregulation of epigenetic process that can influence gene expression and genomic stability. In 4 independent studies in our Bangladesh cohort we have demonstrated that chronic As exposure is associated with increased global DNA methylation, contingent on adequate folate status. We hypothesize that the mechanism underlying this relates to As-induced alterations in histone modifications.

Folate is a key regulator of one-carbon metabolism mediated methylation reactions, including epigenetic modifications such as methylation of DNA and histones. A large randomized trial in Bangladesh has evaluated the effects of folic acid (FA) supplementation on As methylation and blood As concentrations. In this study, we are conducting a cross-disciplinary collaboration that takes advantage of a unique repository of samples collected from this trial to carry out a set of aims related to nutrition/environment interactions. In these aims, we characterize the influence of As exposure on histone modifications, relate changes in histone modifications to changes in DNA methylation, and characterize the impact of FA supplementation on these marks. Finally, using the Infinium Human Methylation450 array, we are identifying a set of genes that are differentially methylated by As exposure and plan to determine expression levels of genes found to be differentially methylated. Collectively, these aims will begin to elucidate the molecular events that underlie the effects of As and folate on DNA methylation. The implications of identifying an influence of FA supplementation on histone modifications are considerable, as this represents a simple, low-cost, low-risk intervention as a potential therapeutic approach to reverse As-induced epigenetic dysregulation.

Project 4. Arsenic, Iron, Sulfur and Organic Carbon Speciation: PI-Ben Bostick

Understanding arsenic mobilization and immobilization requires knowledge of molecular scale processes including mineralogical and microbial studies. Our project focuses on understanding these processes. Over the past year we have further analyzed radiocarbon of DNA from groundwater aquifers and we have compared it to the radiocarbon signature of the phospholipid fatty acids extracted from sediment samples. In addition we have improved our ability to analyze Fe mineralogy from aquifer samples. We coupled standard additions with synchrotron-based X-ray absorption spectroscopy (XAS) to quantify ferrihydrite and magnetite in sediment samples. The combination of XAS and standard-addition enabled us to unambiguously identified ferrihydrite in different aquifer sediments. Furthermore, we have developed better principal components analysis (PCA) to XAS data to better constrain Fe mineralogy, and to extract chemical information such as redox state, and geological information such as sediment source, from these data. These methods enable us to better understand Fe mineralogy which is critical in controlling in arsenic release and movement in arsenic impacted aquifers.

Project 5. Application of Enhanced Mitigation Methods for Groundwater Arsenic at US Superfund Sites: PI-Steve Chillrud

Remediation of arsenic contaminated aquifers has proven difficult. Our project focuses on developing enhanced remediation strategies which could potentially save time and money at Superfund sites contaminated with arsenic. These strategies include oxalic acid injections to improve the efficiency of pump-and-treat at removing arsenic and the immobilization of arsenic into the target mineral magnetite produced via simultaneous addition of ferrous iron and nitrate. The immobilization of groundwater arsenic is a formidable challenge to achieve in part because subsurface geochemical conditions do not favor the long-term stabilization of arsenic on mineral particles. Among many minerals, magnetite is preferable as the target mineral, because it is stable under typical aquifer conditions and important for arsenic sorption. Over the past year, we conducted repeated laboratory batch microcosm experiments with simultaneous addition of ferrous iron and nitrate, and traced the evolution of solution composition and sediment mineralogy/speciation concurrently. We found independent and reproducible confirmation of the formation of arsenic-bearing magnetite which was stable even under sustained Fe(III) reduction. We have also had considerable success modeling our column flow-through experiments to be able to constrain key geochemical parameters for site sediments. These efforts have been integrated with the existing Dover site flow model to develop a reactive transport model (i.e., coupled geochemical and transport simulation) for this magnetite-based strategy. Through such modeling, we identified the geochemical and hydrological processes critical for arsenic sequestration and predicted how spatially and temporally these processes behave at a complex field system. This model will be further amended by field column experiments, and at the same time help design future pilot-scale, field-deployable remediation experiments.

Project 6. Defining the Sustainable Uses of Low-Arsenic Aquifers in Bangladesh: PI-Alexander van Geen

Much of the year was devoted to determining the implications of a blanket survey of close to 50,000 wells in Araihasar using a field kit for arsenic completed in September 2013. About 500 quality-control samples randomly collected under this survey and analyzed in the laboratory have confirmed that the kit correctly classifies wells according to their arsenic content (van Geen et al. 2014). The survey revealed that, sadly, the proportion of wells that meet the WHO guideline of 10 µg/L for arsenic in drinking water or the Bangladesh national standard of 50 µg/L did not increase markedly in Araihasar since the first blanket was conducted under SRP in 2000-01. In addition, the status of about two-thirds of the wells was unknown despite a government-sponsored blanket survey conducted as recently as 2003 because many households have re-installed their wells. The good news resulting from the survey is that with the exception of a handful of wells clustered in 2 villages, the intermediate (>90 m) and deep (>150 m) aquifers of Araihasar turned out to be systematically low in arsenic (van Geen et al., under review). This means that in Araihasar and many (but not all) parts of Bangladesh, the installation of deep community wells can be promoted with increasing confidence. The conclusion is tempered by our finding, again based on the recent blanket survey, that the government subsidies for the installation of 900 deep wells in Araihasar have been poorly allocated. A more even distribution across the most affected villages of the area would have enabled twice as many households with a high-arsenic well to be within walking distance of deep low-arsenic community well. A follow-up to the blanket survey have shown that a small number of deep wells were elevated in arsenic because of leakage through a broken or disconnected PVC pipe using a salt-spiking method (Stahl et al., 2014). A systematic comparison of shallow (<30 m)

wells of Araihasar between 2000-01 and 2012-13 has produced the surprising results that irrigation pumping from this aquifer is homogenizing arsenic concentrations with very little retardation due to adsorption (Mozumder et al. in preparation). The finding suggests shallow low arsenic wells will not remain so indefinitely and justifies further emphasis for study of the deep aquifer.

Beyond the ethical motivation, lowering exposure will help define exposure estimates of the study population in Araihasar and, therefore, the dose-response relationships for various end-points studied under Projects 1, 2, and 3. Our work on the vulnerability of intermediate and deeper aquifers to contamination with As in South Asia is yielding an improved understanding of the impact of groundwater flow on transport of both reactive carbon and arsenic and retardation that is applicable elsewhere, including US Superfund sites.

Administrative Core: Co-PIs-Joseph Graziano and Alexander van Geen

Drs. Graziano and van Geen are involved with other SRP investigators in providing mentorship to the many PhD students involved in our research projects, and work with them to guide their preparation of abstracts and presentations at the annual SRP meeting. Indeed, collectively, our PhD students have presented posters and presentations at numerous national meetings, including the annual SRP meeting, Society of Toxicology meeting, the FASEB summer research conference on folate and one carbon metabolism, the Geological Society of American, the American Society of Agronomy, the Crop Science Society of America, and the Soil Science Society of America.

A meeting of our External Advisory Committee was held on February 25-26, 2013. Our External Advisory Committee continues to provide valuable input to our program. The composition of the committee includes: a) Chien-Jen Chen, Committee Chair, and Chairman of the Graduate Institute of Taiwan; b) Andrew Gelman, Professor of Statistics at Columbia University; c) Zoltan Szabo, Research Hydrologist, USGS; d) Margaret Karagas, Chair, Section of Biostatistics and Epidemiology, Dartmouth University; e) X. Chris Le, Professor of Public Health Sciences, University of Alberta; f) Peggy O'Day, Associate Professor of Natural Sciences, University of California, Merced; and g) Robert Wright, Professor of Preventive Medicine and Pediatrics at the Mount Sinai School of Medicine. The next meeting of the External Advisory Committee will be held on March 9-10 at Columbia University's main campus.

All of our scientific team assembles monthly for a joint two hour meeting which rotates between the Health Sciences Campus and the Lamont-Doherty Earth Observatory Campus; the two campuses are separated by a 20 minute University bus ride. Our monthly meetings include two hours of seminars, typically one hour for biomedical and one for non-biomedical presentations. We also offer our seminars as webinars which are attended by many outsiders from EPA, NIH, DEP and academia. The seminar series includes a mix of internal and external speakers and has evolved into a world class set of events.

Core A. Data Management Core: PI-Diane Levy

During the past year the data management core has overseen the completion of data entry for two major segments of the HEALS study. All data collected for the fourth follow up have been entered into the project database. Additionally, all data collected for the second expansion of the HEALS study have been entered in to the project database. Subsequently, a new data entry system was created to

capture the fifth follow up of the HEALS participants. Those data are being entered now in Dhaka and are being periodically synced with the New York project database. Furthermore, data entry is being done for the Adolescent Study. There are 7 parts to the battery of exams and questionnaires for the study. All data are being coordinated by the data management core so that they reside in the integrated project database. Additionally, all laboratory testing, blood, urine and well water, have been continually uploaded into the project database on a regular basis. Laboratory testing may be initiated by any Superfund project but they are stored centrally for use by any other Superfund investigator. The integration of questionnaire, test and lab data give the investigators the ability to support junior investigators and students in ongoing research.

Core B. Trace Metals Core Laboratory: PI-Joseph Graziano

The primary purpose of the Trace Metals Core Laboratory, which is jointly funded by SRP and our P30 Center, is to provide Center investigators with the capability to obtain analyses of biological samples for a broad array of metals. In addition, the facility provides method development for these analyses, standardization, and quality control. The Trace Metals Core provides analytical support to projects #1, #2 and #3. The Core Laboratories performance in several quality control programs has been outstanding during the past year.

Collectively, during the past year, the lab has performed more than 15,000 measurements of metals in urine, blood, nail and other tissue samples, using either atomic absorption spectrophotometry or inductively coupled plasma mass spectrophotometry (ICP-MS), as needed. A main focus of the Core's activities has been analytical support for As and creatinine measurements for the HEALS Cohort Study (Project #1), which has now completed initiated its fifth biannual follow-up visit. The Trace Metals Core has completed about the analysis of roughly 8,000 urine samples from the first follow-up of the first expansion of the cohort, and roughly 7,000 samples from the baseline of the second cohort expansion. A large portion of ICP-MS running time has been devoted to Dr. Gamble's NIEHS funded RO1 study entitled "Folate and Creatine Supplementation as Therapeutic Approaches to Lowering Blood Arsenic" (FACT study), mainly measuring As metabolites in 4,200 bloods from 600 subjects, i.e., seven time points for each of the 600 subjects. Finally, the lab finished analyses blood, urine and nail arsenic from 300 children in the Bangladesh Child Study follow up (Project #2).

Core C. Biogeochemistry Core Laboratory: PI-Alexander van Geen

The overall purpose of the Biogeochemistry Core is to provide analytical support to 5 of the 6 projects (two biomedical projects and three non-biomedical projects), with additional support for the Community Engagement Core and the Research Translation Core. Over the past year this support has included analysis of approximately 4500 groundwater and leachate samples by ICP-MS, with an additional 3400 QA/QC samples analyzed. Additional analyses include XRF and optical reflectance measurements of soil samples and dissolved organic carbon and dissolved inorganic carbon analyses of sediment incubation and column effluent samples. The method for analysis of exhaled breath condensate samples was moved to a mass spectrometer at Albert Einstein and 100 samples are currently being run for 8-isoprostane for project 2.

Core D. Hydrogeology Core Laboratory: PI-Peter Schlosser

Detailed knowledge of groundwater flow is essential for understanding geochemical processes in the subsurface. Identification of recharge and discharge areas and mechanisms, as well as flow lines are essential for delineating trends in geochemical evolution, including changes in arsenic concentrations, and to quantify reaction rates. Depressurization of the deep, low-arsenic aquifer below our study area of Araihasar in Bangladesh by massive pumping for the municipal water supply of Dhaka has been the focus of non-routine activities supported under Core D. The vast majority of 900+ deep community wells installed throughout Araihasar currently provide water that meets the WHO guideline for arsenic in drinking water but this may not remain the case. The concern is that the pronounced vertical head gradients that have been documented through Core D, in association with Projects 4 and 6, could potentially induce downward flow of shallow high-arsenic groundwater. In addition to the direct observations of water levels in deep wells throughout Araihasar, Core D has contributed to the creation of a hydrogeological model that documents the impact of Dhaka pumping and for the first time, takes into account stratigraphic heterogeneity. Core D also supported the radiocarbon dating of clay samples recovered during the installation of new monitoring wells in Bangladesh, along with chemical analysis of the sediment by X-ray fluorescence.

Core E. Community Engagement Core: PI-Yan Zheng

Community Engagement PI Yan Zheng and USGS Hydrologist Joseph Ayotte together have edited a special issue on arsenic for the journal *Science of the Total Environment (STOTEN)* that will be published on February 1, 2015. Their summary paper, "At the crossroads: Hazard assessment and reduction of health risks from arsenic in private well waters of the northeastern United States and Atlantic Canada" will be the first in a collection of thirteen papers that provides state-of-the-art information on arsenic (As) hydrogeochemistry, effectiveness of household well treatment systems, and the testing and treatment decisions of private well owners in several northeastern U.S. states and in Nova Scotia, Canada. Included in the special issue are two CEC papers reporting the findings of household surveys implemented in Central Maine to identify barriers for private well arsenic testing and treatment. The behavior-influencing factors identified by these surveys are being developed into communication tools that will be tested in the community and guide future efforts for community engagement with domestic well users.

Zheng, Yan and Joseph D. Ayotte. (2015) At the crossroads: Hazard assessment and reduction of health risks from arsenic in private well waters of the northeastern United States and Atlantic Canada. *Science of The Total Environment, Volume 505, Pages 1237-1247*. Available online 18 November 2014, doi:10.1016/j.scitotenv.2014.10.089. PMID: 25466685, PMCID: in process.

Research Translation Core: Co-PI's Steve Chillrud and Meredith Golden

The Columbia Research Translation Core (RTC) focuses on a broad range of government partnerships, including several with the US Environmental Protection Agency (EPA), the Agency for Toxic Substances and Disease Registry (ATSDR), National Institute of Environmental Health Sciences (NIEHS), and local, state, and international agencies concerned with the health impacts and geochemistry of Arsenic (As) and Manganese (Mn) exposures via drinking water, primarily from groundwater in the US and Bangladesh. Together with the Community Engagement Core (CEC) and

Project scientists, the RTC engages in constructive collaborations with those who can benefit from our Center's extensive and integrated biomedical, geoscience, and geospatial expertise. The Columbia RTC widely disseminates, via monthly seminars/webinars, listservers, and numerous conferences, the Center's significant findings and helps to facilitate the timely application of innovative approaches for testing, treatment, and remediation.

Evidence of the "value added" from our RTC efforts over the past year includes that the state of NJ continues to support our partnerships with staff time towards our activities, e.g., a water treatment vendor survey and our fourth educational video (this year on arsenic treatment options for home owners). Furthermore, the state of NJ even provided additional funds and staff time planning and carrying out a joint NJ-RTC-CEC survey of private well owners in northern NJ using the same methodology as the CEC's 2013 household surveys implemented in Maine. At the local government level, Rockland County publically credited RTC's Dr. Braman and his students for providing the county with the evidence-based scientific information necessary for the county to move forward on a water conservation initiative that was passed in June 2014. The objective evidence of the success of our monthly webinars include the attendees from state and federal agencies as well as the requests, such as those from the director of the NIEHS Dr. Linda Birnbaum, for copies of the presentations. In addition, our RTC's expertise with GIS and geospatial data has continued to be sought out in 2014 for our work on the NPL Superfund Footprint Mapper as well as to potentially host interagency workshops and discussions. Finally, our investigator team has carried out a wide array of research translation activities in the US and Bangladesh. Here we highlight two: first the National Research Council (NRC) Interim Report on "Critical Aspects of EPA's IRIS Assessment of Inorganic Arsenic" was released in 2014. It was the culmination of a NRC committee chaired by Dr. Graziano with input from a number of our scientists. Second, Dr. Graziano together with Columbia SRP scientists Drs. van Geen, Parvez and Matin summarized and discussed the key findings of Columbia's 15 years of arsenic research in Bangladesh at a meeting with the Bangladesh Medical Research Council (BMRC) and the Bangladesh Minister of Health on 17 June 2014.

E. Project/Core Publications

Project 1.

1: Wu F, Jasmine F, Kibriya MG, Liu M, Cheng X, Parvez F, Islam T, Ahmed A, Rakibuz-Zaman M, Jiang J, Roy S, Paul-Brutus R, Slavkovich V, Islam T, Levy D, VanderWeele TJ, Pierce BL, Graziano JH, Ahsan H, Chen Y. Interaction between Arsenic Exposure from Drinking Water and Genetic Polymorphisms on Cardiovascular Disease in Bangladesh: A Prospective Case-Cohort Study. *Environ Health Perspect.* 2015 Jan 9. [Epub ahead of print] PMID: 25575156.

2: Gao J, Roy S, Tong L, Argos M, Jasmine F, Rahaman R, Rakibuz-Zaman M, Parvez F, Ahmed A, Hore SK, Sarwar G, Slavkovich V, Yunus M, Rahman M, Baron JA, Graziano JH, Ahsan H, Pierce BL. Arsenic exposure, telomere length, and expression of telomere-related genes among Bangladeshi individuals. *Environ Res.* 2015 Jan;136:462-9. doi: 10.1016/j.envres.2014.09.040. Epub 2014 Nov 25. PMID: 25460668; PMCID: PMC4264833.

3: Argos M, Chen L, Jasmine F, Tong L, Pierce BL, Roy S, Paul-Brutus R, Gamble MV, Harper KN, Parvez F, Rahman M, Rakibuz-Zaman M, Slavkovich V, Baron JA, Graziano JH, Kibriya MG, Ahsan H. Gene-specific differential DNA methylation and chronic arsenic exposure in an epigenome-wide association study of adults in Bangladesh. *Environ Health Perspect.* 2015 Jan;123(1):64-71. doi: 10.1289/ehp.1307884. Epub 2014 Oct 17. PMID: 25325195; PMCID: PMC4286273.

- 4: Scannell Bryan M, Argos M, Pierce B, Tong L, Rakibuz-Zaman M, Ahmed A, Rahman M, Islam T, Yunus M, Parvez F, Roy S, Jasmine F, Baron JA, Kibriya MG, Ahsan H. Genome-wide association studies and heritability estimates of body mass index related phenotypes in Bangladeshi adults. *PLoS One*. 2014 Aug 18;9(8):e105062. doi: 10.1371/journal.pone.0105062. eCollection 2014. PMID: 25133637; PMCID: PMC4136799.
- 5: Mozaffarian D, Fahimi S, Singh GM, Micha R, Khatibzadeh S, Engell RE, Lim S, Danaei G, Ezzati M, Powles J; Global Burden of Diseases Nutrition and Chronic Diseases Expert Group. Global sodium consumption and death from cardiovascular causes. *N Engl J Med*. 2014 Aug 14;371(7):624-34. doi: 10.1056/NEJMoa1304127. PMID: 25119608. Free full text: <http://www.nejm.org/doi/full/10.1056/NEJMoa1304127>
- 6: Pesola GR, Ahsan H. Dyspnea as an independent predictor of mortality. *Clin Respir J*. 2014 Jul 28. doi: 10.1111/crj.12191. [Epub ahead of print] PMCID: PMC4309743
- 7: Argos M, Parvez F, Rahman M, Rakibuz-Zaman M, Ahmed A, Hore SK, Islam T, Chen Y, Pierce BL, Slavkovich V, Olopade C, Yunus M, Baron JA, Graziano JH, Ahsan H. Arsenic and lung disease mortality in Bangladeshi adults. *Epidemiology*. 2014 Jul;25(4):536-43. doi: 10.1097/EDE.000000000000106. PMID: 24802365. NIHMSID: 660748
- 8: Zheng W, McLerran DF, Rolland BA, Fu Z, Boffetta P, He J, Gupta PC, Ramadas K, Tsugane S, Irie F, Tamakoshi A, Gao YT, Koh WP, Shu XO, Ozasa K, Nishino Y, Tsuji I, Tanaka H, Chen CJ, Yuan JM, Ahn YO, Yoo KY, Ahsan H, Pan WH, Qiao YL, Gu D, Pednekar MS, Sauvaget C, Sawada N, Sairenchi T, Yang G, Wang R, Xiang YB, Ohishi W, Kakizaki M, Watanabe T, Oze I, You SL, Sugawara Y, Butler LM, Kim DH, Park SK, Parvez F, Chuang SY, Fan JH, Shen CY, Chen Y, Grant EJ, Lee JE, Sinha R, Matsuo K, Thornquist M, Inoue M, Feng Z, Kang D, Potter JD. Burden of total and cause-specific mortality related to tobacco smoking among adults aged ≥ 45 years in Asia: a pooled analysis of 21 cohorts. *PLoS Med*. 2014 Apr 22;11(4):e1001631. doi: 10.1371/journal.pmed.1001631. eCollection 2014 Apr. PMID: 24756146; PMCID: PMC3995657.
- 9: Micha R, Khatibzadeh S, Shi P, Fahimi S, Lim S, Andrews KG, Engell RE, Powles J, Ezzati M, Mozaffarian D; Global Burden of Diseases Nutrition and Chronic Diseases Expert Group NutriCoDE. Global, regional, and national consumption levels of dietary fats and oils in 1990 and 2010: a systematic analysis including 266 country-specific nutrition surveys. *BMJ*. 2014 Apr 15;348:g2272. doi: 10.1136/bmj.g2272. PMID: 24736206; PMCID: PMC3987052.
- 10: Chen Y, Ge W, Parvez F, Bangalore S, Eunos M, Ahmed A, Islam T, Rakibuz-Zaman M, Hasan R, Argos M, Levy D, Sarwar G, Ahsan H. A prospective study of arm circumference and risk of death in Bangladesh. *Int J Epidemiol*. 2014 Aug;43(4):1187-96. doi: 10.1093/ije/dyu082. Epub 2014 Apr 7. PMID: 24713183; PMCID: PMC4121562.
- 11: Argos M, Tong L, Pierce BL, Rakibuz-Zaman M, Ahmed A, Islam T, Rahman M, Paul-Brutus R, Rahaman R, Roy S, Jasmine F, Kibriya MG, Ahsan H. Genome-wide association study of smoking behaviours among Bangladeshi adults. *J Med Genet*. 2014 May;51(5):327-33. doi: 10.1136/jmedgenet-2013-102151. Epub 2014 Mar 24. PMID: 24665060; PMCID: PMC4126189.
- 12: Wu F, Jasmine F, Kibriya MG, Liu M, Cheng X, Parvez F, Paul-Brutus R, Paul RR, Sarwar G, Ahmed A, Jiang J, Islam T, Slavkovich V, Rundek T, Demmer RT, Desvarieux M, Ahsan H, Chen Y. Interaction between arsenic exposure from drinking water and genetic susceptibility in carotid intima-media thickness in Bangladesh. *Toxicol Appl Pharmacol*. 2014 May 1;276(3):195-203. doi: 10.1016/j.taap.2014.02.014. Epub 2014 Mar 2. PMID: 24593923; PMCID: PMC4080412.

13: McClintock TR, Parvez F, Wu F, Wang W, Islam T, Ahmed A, Shaheen I, Sarwar G, Demmer RT, Desvarieux M, Ahsan H, Chen Y. Association between betel quid chewing and carotid intima-media thickness in rural Bangladesh. *Int J Epidemiol*. 2014 Aug;43(4):1174-82. doi: 10.1093/ije/dyu009. Epub 2014 Feb 17. PMID: 24550247; PMCID: PMC4121551.

14: McClintock TR, Chen Y, Parvez F, Makarov DV, Ge W, Islam T, Ahmed A, Rakibuz-Zaman M, Hasan R, Sarwar G, Slavkovich V, Bjurlin MA, Graziano JH, Ahsan H. Association between arsenic exposure from drinking water and hematuria: results from the Health Effects of Arsenic Longitudinal Study. *Toxicol Appl Pharmacol*. 2014 Apr 1;276(1):21-7. doi: 10.1016/j.taap.2014.01.015. Epub 2014 Jan 28. PMID: 24486435; PMCID: PMC3959280.

Oral presentations:

1. Gene-Environment Interactions between Arsenic Exposure from Drinking Water and Genetic Susceptibility in Cardiovascular Disease Risk and Carotid Artery Intima-Media Thickness in Bangladesh. The 5th International Congress on Arsenic in the Environment – “One century of the discovery of arsenicosis in America (1913-2014)”. May 2014, Buenos Aires, Argentina.

2. Arsenic, the Gut Microbiome, and Atherosclerosis. International Society of Environmental Epidemiology Annual Meeting. August, 2014. Seattle, USA.

3. Interaction Between Arsenic Exposure From Drinking Water and Genetic Susceptibility in Cardiovascular Disease Risk and Carotid Artery Intima-Media Thickness in Bangladesh. International Society of Environmental Epidemiology Annual Meeting. August, 2014. Seattle, USA.

4. Arsenic exposure and the risk of preclinical and clinical endpoints of cardiovascular disease. International Congress of Toxicology. November 29- 30, 2014. Ankara, Turkey.

Project 2.

Wasserman, G, Liu, X, Lolacono, N, Kline, J, Factor-Litvak, P, van Geen, A, Mey, JL, Levy, D, Abramson, R, Schwartz, A, Graziano, JH: A cross-sectional study of well water arsenic and child IQ Maine schoolchildren. *Environ Health* 2014 April 1;13(1):23. Doi:10.1186/1476-069X-13-23. PMCID: PMC4104994

Khan K, Ahmed E, Factor-Litvak P,1 Liu X,1 Siddique AB, Wasserman GA, Slavkovich V, Levy D, Mey JL, van Geen A, Graziano JH. Evaluation of an Elementary School-based Educational Intervention for Reducing Arsenic Exposure in Bangladesh. Under review of minor revisions, *Environ Health Perspect*, Jan 2015.

Wasserman, GA, Liu, X, Parvez, F, Factor-Litvak, P, Kline, J, Siddique, AB, Shahriar, H, Nasiruddin, M, van Geen, A, Mey, J, Balac, O, Graziano, JH: Reducing Well water As Exposure and changes in child intelligence, about to be submitted.

Oral Presentation:

Sanchez, T., Siddique, A., Shahriar, M., Uddin, M., Lomax-Luu, A., Levy, D., Graziano, J., van Geen, A. & Gamble, M. (November 2014) Limited impact of point-of-use filters on arsenic exposure in the Folate

and Creatinine Trial (FACT). Poster presented at the Superfund Research Program Annual Meeting, San Jose, CA.

Project 3.

Lawley SD, Yun J, Gamble MV, Hall MN, Reed MC, Nijhout HF. Mathematical modeling of the effects of glutathione on arsenic methylation. *Theor Biol Med Model.* 2014 May 16;11:20 PMID: PMC4041632.

Howe C, Niedzwiecki MM, Hall MN, Liu X, Ilievski V, Slavkovich V, Alam S, Siddique A, Graziano JH and Gamble MV. Folate and cobalamin modify associations between s-adenosylmethionine and methylated arsenic metabolites in arsenic-exposed Bangladeshi adults. *Journal of Nutrition.* 2014 May; 144(5):690-7. PMID:PMC3985826.

Harper K, Liu X, Hall MN, Ilievski V, Oka J, Calancie L, Slavkovich V, Levy D, Siddique A, Alam S, Mey JL, van Geen A, Graziano JH and Gamble MV. A dose-response study of arsenic exposure and markers of oxidative damage in Bangladesh. *J Occup Environ Med* 2014 Jun;56(6):652-8. PMID:PMC4050339.

Niedzwiecki MM, Hall MN, Liu X, Slavkovich V, Ilievski V, Levy D, Alam S, Siddique A, Parvez F, Graziano JH and Gamble MV. Interaction of plasma glutathione redox and folate deficiency on arsenic methylation capacity in Bangladeshi adults. *Free Radical Biology and Medicine.* 2014 Aug; 73:67-74. PMID:PMC4111991.

Peters BA, Hall MN, Liu X, Neugut YD, Pilsner JR, Levy D, Ilievski V, Slavkovich V, Islam T, Factor-Litvak P, Graziano JH and Gamble MV. Creatinine, arsenic metabolism and renal function in an arsenic-exposed population in Bangladesh. *PlosOne* (in press).

Oral/Poster Presentations

Dr. Gamble's laboratory was well represented at The FASEB Summer Research Conference on Folate and One Carbon Metabolism in Steamboat Springs, CO, in August 2014. Four members of Dr. Gamble's group presented. The presentations were as follows:

- Megan N. Hall, invited oral presentation: "Folic acid and creatine as therapeutic approaches to lowering blood arsenic concentrations: A randomized controlled clinical trial."
- Megan Niedzwiecki, invited oral presentation: "Influences of arsenic, homocysteine, and gender on global 5-methylcytosine and 5-hydroxymethylcytosine content of human white blood cell DNA"
- Brandilyn Peters, invited oral presentation: "Interactions between inflammatory biomarkers and circulating intermediates of one-carbon metabolism."
- Caitlin Howe, poster presentation: "Homocysteine is associated with %H3K36me2, independent of folate, cobalamin, SAM, and SAH"

November 12 to 14, 2014, attend the Superfund Research Program's Annual Meeting in San Jose, CA. Dr. Gamble's laboratory was represented by the following presentations:

- Megan N. Hall presented a poster on Dr. Gamble's study entitled, "Folic acid and creatine as therapeutic approaches to lowering blood arsenic concentrations: A randomized controlled clinical trial."

- Tiffany Sanchez, Dr. Gamble & Dr. Graziano's PhD student, presented a poster entitled, "Limited impact of point-of-use filters on arsenic exposure in the Folate and Creatine Trial (FACT)."

Project 4.

Wovkulich, K, M. Stute, B.J. Mailloux, A.R. Keimowitz, J. Ross, B.C. Bostick, J. Sun, and S.N. Chillrud. In Situ Oxalic Acid Injection to Accelerate Arsenic Remediation at a Superfund Site in New Jersey. *Environmental Chemistry*, 2014, 11(5): 525-537. PMID:25598701 PMCID: PMC4294815

Layton, A; A Chauhan, D Williams, B Mailloux, P Knappett, A Ferguson, L Mckay, MJ Alam, KM Ahmed, A van Geen, G Saylor. Metagenomes of microbial communities in arsenic and pathogen contaminated well and surface water from Bangladesh. *Genome Announcements (genomeA)*. Accepted October 2014.

Sun J, S.N. Chillrud, B.J. Mailloux, M. Stute, R. Singh, H. Dong, C. Lepre, and B.C. Bostick. Enhanced Arsenic Retention in Microcosms Containing Magnetite Formed Through the Oxidation of Ferrous Iron by Nitrate. Submitted.

Presentations

J. Sun. Arsenic In-Situ Immobilization by Magnetite Formation within Contaminated Aquifer Sediments. Superfund Trainee Webinar Series on April 30, 2014.

J. Sun, B.J. Mailloux, S.N. Chillrud, and B.C. Bostick. Quantifying Ferrihydrite in Soils and Sediments Using Standard-Addition Methods Applied to X-Ray Absorption Spectroscopy. Oral Presentation at the 2014 ASA-CSSA-SSSA International Annual Meetings. Won 3rd Place Student Presentation Award for the Soil Chemistry division.

Bostick, Benjamin C. Alternatives to Arsenic-Contaminated Groundwater: A Case for Piped Water in Rural Cambodia. Oral Presentation at the 2014 GSA Annual Meeting in Vancouver, British Columbia.

Knappett, Peter S.K., Akhter, Syed H., Choudhury, Imtiaz, Steckler, Michael, Michael, Holly A., Harvey, Charles F., Ahmed, Kazi Matin, Bostick, Benjamin C., Shamsudduha, M., and van Geen, A. Impact of Over Pumping from Deep Aquifer in Dhaka City on the Safe water supply for the Surrounding Rural Population. Oral Presentation at the 2014 GSA Annual Meeting in Vancouver, British Columbia.

Khan, Mahfuzur R., Koneshloo, Mohammad, Knappett, Peter S.K., Mozumder, M. Rajib Hassan, Mailloux, Brian, Ahmed, Kazi Matin, Bostick, Benjamin C., Harvey, Charles F., van Geen, Alexander, and Michael, Holly A. Effect of Aquifer heterogeneity on the sustainability of deep groundwater resources in the Bengal Delta near a mega-city pumping center. Oral Presentation at the 2014 GSA Annual Meeting in Vancouver, British Columbia.

Project 5.

K. Wovkulich, M. Stute, B.J. Mailloux, A.R. Keimowitz, J. Ross, B.C. Bostick, J. Sun, and S.N. Chillrud. In Situ Oxalic Acid Injection to Accelerate Arsenic Remediation at a Superfund Site in New Jersey. *Environmental Chemistry*, 2014, 11(5): 525-537. PMCID: PMC4294815

J. Sun. Arsenic In-Situ Immobilization by Magnetite Formation within Contaminated Aquifer Sediments. Superfund Trainee Webinar Series on April 30, 2014.

J. Sun, B.J. Mailloux, S.N. Chillrud, and B.C. Bostick. Quantifying Ferrihydrite in Soils and Sediments Using Standard-Addition Methods Applied to X-Ray Absorption Spectroscopy. Oral Presentation at the 2014 ASA-CSSA-SSSA International Annual Meetings. Won 3rd Place Student Presentation Award for the Soil Chemistry division.

J. Sun, S.N. Chillrud, B.J. Mailloux, M. Stute, R. Singh, H. Dong, C. Lepre, and B.C. Bostick. Enhanced Arsenic Retention in Microcosms Containing Magnetite Formed Through the Oxidation of Ferrous Iron by Nitrate. Submitted.

Project 6.

Layton, A; A Chauhan, D Williams, B Mailloux, P Knappett, A Ferguson, L Mckay, MJ Alam, KM Ahmed, A van Geen, G Saylor. Metagenomes of microbial communities in arsenic and pathogen contaminated well and surface water from Bangladesh. *Genome Announcements* *Genome Announc.* 2014 Nov-Dec; 2(6): e01170-14. PMID: PMC4239352

Wasserman GA, Liu X, Kline J, Factor-Litvak P, Lolocono N, van Geen A, Mey JL, Levy D, Abramson R, Schwartz A, Graziano JH, Exposure to arsenic from household wells and intelligence, in Maine schoolchildren. *Environmental Health* 13:23, 2014. PMID: PMC4104994

Stahl, MO, JB Ong, CF Harvey, CD Johnson, ABM Badruzzaman, MH Tarek, A. van Geen, JA Anderson, JW Lane. Detecting well casing leaks in Bangladesh using a salt spiking method. *Groundwater* 52, 195–200, 2014. doi: 10.1111/gwat.12200. PMID in process.

Harper, K.N., X. Liu, M.N. Hall, V. Ilievski, J. Oka, L. Calancie, V. Slavkovich, D. Levy, J.L. Mey, A. van Geen, J.H. Graziano, M.V. Gamble. A dose-response study of arsenic exposure and markers of oxidative damage in Bangladesh. *J Occup Environ Med* 652-8, 2014. PMID:PMC4050339

van Geen A, EBA Sumon, L Pitcher, JL Mey, H Ahsan, JH Graziano, KM Ahmed. Comparison of two blanket surveys of arsenic in tubewells conducted 12 years apart in a 25 km² area of Bangladesh. *Sci Tot Environ* 488-489: 484-92, 2014. PMID: PMC4043877.

van Geen A, KH Win, T Zaw, W Naing, JL Mey, B Mailloux. Confirmation of elevated arsenic levels in groundwater of Myanmar. *Sci Tot Environ* 478: 21-24, 2014. PMID: PMC3954970.

van Geen A, KM Ahmed, EB Ahmed, I Choudhury, MR Mozumder, BC Bostick, BJ Mailloux. Increasing the impact of deep-well installations to reduce arsenic exposure in Bangladesh. Submitted to *Environ Sci & Technol*, November 2014.

Peters, BA, MN Hall, X Liu, P Factor-Litvak, F Parvez, A van Geen, JL Mey, AB Siddique, MH Shahriar, MN Uddin, MT Islam, V Slavkovich, V Ilievski, JH Graziano, MV Gamble. Folic acid and creatine as therapeutic approaches to lower blood arsenic: A randomized-controlled trial. Submitted to *Environ Health Perspect*, October 2014.

Pfaff A, Schoenfeld A, Ahmed KM, van Geen A. Reducing arsenic exposure in Bangladesh: New evidence of the impacts of insufficient testing and health-risk communication from a tubewell and household survey. Submitted to *J Health, Population & Nutr*, October 2014.

Knappett, PSK, BJ Mailloux, I Choudhury, M Khan, H Michael, S Barua, DR Mondal, M Steckler, H Akter, KM Ahmed, B Bostick, C Harvey, M Shamsudduha, I Mihajlov, R Mozumder, A. van Geen. Vulnerability of intermediate and deep low-arsenic aquifers to municipal pumping in Bangladesh. Revision submitted to *Environ Sci & Technol*, December 2014.

Khan K, EB Ahmed, P Factor-Litvak, X Liu, Z Rahman, HA Ferdous, AB Siddique, GA Wasserman, V Slavkovich, D Levy, J Mey, A van Geen, JH Graziano. Evaluation of an elementary school-based educational intervention for reducing arsenic exposure in Bangladesh. *Environ Health Perspect*, under review for minor revisions, January 2015.

Mozumder MR, EB Ahmed, KM Ahmed, BC Bostick, BJ Mailloux, A Geen. Homogenization of groundwater arsenic concentrations in shallow reducing aquifers over time: Evidence from two well surveys conducted twelve years apart in Arahazar, Bangladesh. In preparation for *Environ Sci & Technol*, Jan 2015.

Cores A-D

There are no unique core specific publications from these cores but the publications from the projects above heavily rely on their contributions.

Core E.

Zheng, Yan and Joseph D. Ayotte. (2015) At the crossroads: Hazard assessment and reduction of health risks from arsenic in private well waters of the northeastern United States and Atlantic Canada. *Sci Total Environ*, 2015 Feb 1;505:1237-47. doi:10.1016/j.scitotenv.2014.10.089. PMID: 25466685, PMCID: in process.

Flanagan, S.V., Marvinney, R.G., Johnston, R.A., Yang, Q., Zheng, Y. (2015) Dissemination of well water arsenic results to homeowners in Central Maine: Influences on mitigation behavior and continued risks for exposure. *Sci Total Environ*, 2015 Feb 1;505: 1282-90. doi:10.1016/j.scitotenv.2014.03.079. PMCID: PMC4192113

Flanagan, S.V., Marvinney, R.G., and Zheng, Y. (2015) Influences on domestic well water testing behavior in a Central Maine area with frequent groundwater arsenic occurrence. *Sci Total Environ*, 2015 Feb 1;505: 1274-81. doi:10.1016/j.scitotenv.2014.05.017. PMCID: PMC4245378

Presentations

Flanagan, S.V. and Y. Zheng (2014, May). Arsenic exposure through well water and household behavior in a rural Maine community: Implications for mitigation. Poster presented at the 5th International Congress on Arsenic in the Environment. Buenos Aires, Argentina.

*Winner of poster contest for Theme 5: Mitigation Management and Policy.

Research Translation Core

Golden, M. and T. Chai-Onn. (February 2014). The Columbia University Superfund Research Program's NPL Superfund Footprint Mapper. U.S. EPA Sustainable and Healthy Communities (SHC) Seminar Series webinar.

Flanagan, S.V., presenter. (May 2014). Arsenic exposure through well water and household behavior in a rural Maine community: Implications for mitigation. Poster presented at the 5th International Congress on Arsenic in the Environment. Buenos Aires, Argentina.

*Winner of poster contest for Theme 5: Mitigation Management and Policy.

Braman, S., presenter. (November 2014). Building Partnerships between Local and State Government Agencies and the RTC and CEC-- Time, Effort and Outcomes. RT/CE Partnership Poster Session. SRP Annual Meeting, San Jose, CA.

Chai-Onn, T and M. Golden. (December 2014). Superfund Site Footprints Data with metadata for direct download (<http://sedac.ciesin.columbia.edu/data/collection/superfund/sets/browse>): ATSDR Hazardous Waste Site Polygon Data, v2 (2010), 2.1 MB zipped shapefile, <http://dx.doi.org/10.7927/H48P5XF7>; ATSDR Hazardous Waste Site Polygon Data with CIESIN Modifications, v2 (2010), 1.4 MB zipped shapefile, <http://dx.doi.org/10.7927/H4DF6P5Z>; and U.S. EPA National Priorities List Sites with CIESIN Modifications, v2 (2014), 728 KB xls file, <http://dx.doi.org/10.7927/H44X55RB>. Disseminated online by NASA Socioeconomic Data and Applications Center (SEDAC) hosted by Center for International Earth Science Information Network - CIESIN - Columbia University, Palisades, NY.