

**Columbia University Superfund Basic Research Program
Annual Project and Core Updates – 2010**

Health Effects and Geochemistry of Arsenic and Manganese

Director: Joseph H. Graziano

Deputy Director: Alexander van Geen

Highlight #1: Adverse Effects of Arsenic Exposure on Motor Function in 7-9 Year-Old Children in Bangladesh

PI: Joseph Graziano, PhD

We and others have previously documented the adverse impact of chronic exposure to elevated levels of well-water As on children's intellectual function. We have also documented decrements in intellectual functioning in 10-year-olds exposed to elevated levels of well-water Mn in a region of Bangladesh where water As levels were extremely low. That work, however, was not designed to examine possible interactive effects of simultaneous exposure to both As and Mn. Accordingly, in order to allow investigation of the possible synergistic impact of both exposures, we recruited a new sample of children from a neighboring region, stratified by design on As and Mn concentrations of household wells. We investigated the impact of these co-exposures on child intelligence (reported elsewhere) and motor function, which has not previously been studied.

The parents of the children in this study are participants in our large ongoing prospective longitudinal study of adults, i.e., the Health Effects of Arsenic Longitudinal Study (HEALS). Following a survey of the well characteristics of HEALS cohort villages within commuting distance of our field clinic, we designated household wells into one of four groups: High As High Mn (HAs-HMn: As > 10 µg/L and Mn > 400 µg/L), High As Low Mn (HAs-LMn), Low As High Mn (LAs-HMn) and Low As Low Mn (LAs-LMn). The cutoff values of 10 and 400 ppb, respectively, represent the WHO guideline values for drinking water.

We identified all children estimated to be between 8 and 11 years old and continued recruitment at random until approximately 75 were included in each well category group. Urine samples were collected for the measurement of urinary arsenic (UAs) and creatinine; toenails for As and Mn; and blood for the measurement of whole blood arsenic (BAs), lead (BPb), manganese (BMn), and selenium (BSe) and plasma ferritin. All children were evaluated on tests of intelligence (reported elsewhere) and motor function, using the Bruininks-Oseretsky Test (BOT-2), an individually-administered test that measures a wide range of motor skills in children. BOT-2 is made up of four motor area composites: fine manual control (FMC), manual coordination (MC), body coordination (BC) and strength and agility (SA) and one comprehensive measure of overall motor proficiency, total motor composite (TMC).

As expected, sociodemographic factors made consistent contributions to measures of each subtest, both before and after adjustment. Boys, children with larger head circumferences and those with longer school attendance achieved significantly higher scores on the TMC (all p 's < .05). A consistent positive effect of male gender was observed on all the sub-scales (all p 's < 0.0001). Head circumference was positively associated with FMC (β = 0.77, p < 0.05) and BC (β = 0.67, p < 0.01), while children with higher plasma ferritin levels (>32.5 ng/ml) did significantly better on TMC (β = 5.01, p < 0.01), MC and BC. We also have observed a strong positive association between BSe and overall motor function, a novel finding. A significant association between BSe and TMC (β = 3.54, p < 0.005), FMC (β = 1.55, p < 0.005) and MC (β = 1.57, p < 0.005) was apparent in the unadjusted models. Interestingly, the positive association between BSe and TMC (β = 1.57, p < 0.005) and two of the sub-scales, FMC (β = 1.57, p < 0.005) and MC (β = 1.57, p < 0.005), remained significant when adjusted for blood As, Mn, and Pb.

In unadjusted linear regression models, strong inverse associations were observed between BAs and TMC (β = -3.78, p < 0.01), FMC (β = -1.94, p < 0.01) and BC (β = -1.38, p < 0.01). These inverse associations remained highly significant after adjustment for sociodemographic covariates: TMC (β = -3.54, p < 0.01), FMC (β = -1.50, p < 0.05) and BC (β = -1.59, p < 0.01).

Strong inverse associations between other measures of As exposure (Water As, UAs, and toenail As) and motor function were also observed. In contrast, Mn exposure, as assessed by BMn and well water Mn concentrations were *not* related to any of the subtests on the BOT-2 either before or after adjustment for covariates. Results for As exposure are consistent with commonly reported findings in adults with serious arsenic poisoning. These novel findings concerning adverse effects of As on motor function, coupled with past reports concerning the adverse impact of As exposure on intelligence, add a new sense of urgency to the problem of As exposure in children.

Highlight #2: Application of Mathematical Modeling of One-carbon Metabolism to Study Nutritional Influences on Arsenic Methylation

PI: Mary Gamble, PhD

Roughly 140 million people worldwide are exposed to arsenic (As)-contaminated drinking water. Arsenic is a class I carcinogen known to cause several cancers. Metabolism of inorganic As (InAs), which facilitates urinary excretion, relies on one-carbon metabolism (OCM) and involves two methylation steps; both utilize S-adenosylmethionine (SAM) as the methyl donor. InAs is methylated to monomethylarsonic acid (MMAs) which can undergo a second methylation to dimethylarsinic acid (DMAs). Our previous work in Bangladesh has revealed a high prevalence of folate deficiency, and has shown that folic acid supplementation to folate-deficient adults increases As methylation and lowers blood As. These findings lend support to the hypothesis that nutritional interventions may decrease the adverse health effects of As exposure. However, a purely epidemiologic approach yields a limited understanding of the overall functioning of the OCM system in relation to As methylation. In a new collaboration with biologist Fred Nijhout, mathematicians Mike Reed and Sean Lawley, from Duke University, and with support from our SRP and an NIEHS K99/R00 award to epidemiologist Megan Hall, we are using mathematical modeling to: 1) provide further insight into our previous findings on folate supplementation and arsenic methylation; and 2) make predictions about how to best improve arsenic methylation through other nutritional approaches.

We developed a whole body mathematical model of As metabolism, including parameters for absorption, storage, methylation, and excretion. Model parameters were taken from the literature when possible. For example, we used Michaelis-Menten constants for arsenic (+3 oxidation state) methyltransferase (AS3MT) from Wood et al (2006). The remaining parameters were tuned by fitting the single dose human experiments in Buchet et al (1981a). Functions that provided the level of arsenic in each compartment at any time were derived using a system of ordinary differential equations. Mathematical software (MATLAB) was used to solve the system. We then compared the model predictions to the multiple dose experiments in Buchet et al (1981b) and used the model to explain our previous findings in Bangladesh on the effects of folate supplementation on arsenic methylation in a folate-deficient population.

We compared model output to the data from Buchet et al (1981b) in which human volunteers were given 1000, 500, 250, or 125 μg InAs /day for 5 days and urinary As metabolites were measured every 24 hrs for 2 weeks. For each dose of InAs, the predicted uAs metabolite excretion rates from our model were quite close to the excretion rates from the experimental data. We then modified the model slightly to account for lower concentrations of SAM in the folate-deficient Bangladeshi population, and the rate of the velocity of AS3MT reaction in a chronically exposed population as opposed to the acute dosing experiments of Buchet et al.

The model accurately predicts the distribution of urinary and blood As metabolites in the folate-deficient population before folate supplementation:

	Inorganic As	MMAs	DMAs
blood (Gamble data)	26%	40%	34%
blood (model)	26%	39%	35%
urine (Gamble data)	15%	13%	72%
urine (model)	15%	15%	69%

The model also accurately predicts the percentages of urinary and blood As metabolites observed in our clinical trial after folic acid supplementation:

	Inorganic As	MMAs	DMAs	Total (% change)
blood (Gamble data)	23%	37%	40%	-14%
blood (model)	22%	33%	45%	-13%
urine (Gamble data)	10%	11%	79%	
urine (model)	11%	11%	77%	
liver (model)				-19%
body (model)				-26%

A huge advantage of the mathematical model is that it permits us to estimate the effect of the intervention **on body stores of arsenic**. **The model actually estimates that folic acid supplementation achieves remarkable reductions in liver stores of arsenic by 19% and total body stores by 26%.**

Ultimately, this model will allow the rapid conduct of multiple *in silico* experiments to 1) investigate the effects of other nutritional interventions on As methylation, 2) investigate how nutrients interact to influence As methylation, and 3) facilitate an improved understanding of the mechanisms underlying our experimental findings, e.g. increased hepatic SAM concentrations. The knowledge gained will lead to more targeted nutritional interventions to improve As methylation and lower body stores of arsenic. In comparison to even small pilot studies in human populations, this model is an extraordinarily cost-effective means of testing new hypotheses.

References:

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Highlight #3: Association between chronic arsenic exposure and blood glutathione concentrations in Bangladesh.

PI: Mary Gamble, PhD

Background: Chronic arsenic (As) exposure is associated with increased risk for several types of cancer as well as heart disease. However, the mechanisms through which As causes disease are poorly understood. *In vitro* and animal studies have shown that As induces oxidative stress, i.e., an imbalance between the production of reactive oxygen and the ability to readily detoxify the reactive intermediates or easily repair the resulting damage. However, research in human populations is sparse. Glutathione (GSH) serves as a cornerstone of the primary endogenous antioxidant defense mechanisms and also is the electron donor for InAs reduction. It is a tri-peptide comprised of glycine, glutamic acid, and cysteine (Cys). GSH is the most abundant nonprotein thiol in the cell, and the content of GSH is exquisitely sensitive to changes in redox status (1). GSH also serves to provide a source of Cys to maintain overall sulfur amino acid balance; due to its high reactivity, only low concentrations of Cys can be tolerated in cells (2). Cysteine (Cys) is an important and sometimes limiting substrate for GSH biosynthesis and Cys and cystine (CySS) are the major redox couple in plasma (3). Studies in mice given arsenic in drinking water found that As exposure induced elevated hepatic GSH at two months but significantly reduce hepatic GSH at four months, reflecting an initial defense response which eventually cannot be sustained (4). These results are consistent with rat studies which have shown that As decreases hepatic concentrations of GSH (5). Arsenic and GSH metabolism are linked and As may influence GSH status by: 1) inducing the formation of reactive oxygen species (ROS) (6;7), 2) binding to and eventually depleting GSH (8), and 3) inhibiting the enzyme glutathione reductase (9), which regenerates GSH from glutathione disulfide (GSSG), the product of GSH reduction of ROS. Given that many environmental exposures, including many drugs, stimulate oxidative stress, we sought to determine the impact of As exposure on GSH in a human population.

New Novel Findings in Humans: A cross-sectional study in Bangladesh was designed to evaluate the relationship between chronic As exposure and blood and plasma concentrations of glutathione. A sample of 379 participants between the ages of 30 and 63 were recruited based on 5 categories of arsenic exposure. The distribution of water arsenic exposure in the study participants was as follows: <10 (n=76), 10-100 (n=104), 101-200 (n=86), 201-300 (n=67), and >300 (n=45) µg/L. Whole blood and plasma GSH and GSSG and plasma Cys and CySS were derivatized immediately after sample collection in the field and their concentrations were measured using high performance liquid chromatography with fluorescence detection. The associations between arsenic exposure as measured by water, urine and blood As with the glutathione outcomes are tabulated below.

Parameter estimates ^a for associations between water/urinary/blood arsenic and GSH outcomes.						
	Water Arsenic		Urinary Arsenic		Blood Arsenic	
	b	p-value	b	p-value	b	p-value
Plasma GSH ^b	0.0005	0.95	0.00017	0.99	-0.006	0.74
Plasma GSSG ^b	-0.001	0.85	0.008	0.61	0.005	0.80
Plasma GSH Eh	-0.023	0.87	0.10	0.81	0.22	0.63
Blood GSH	-0.17	< 0.0001	-44.3	< 0.0001	-46.4	< 0.0001
Blood GSSG ^b	0.005	0.97	-0.003	0.90	0.002	0.96
Blood GSH:GSSG ^b	-0.04	0.01	-0.10	0.008	-0.11	0.007
Blood GSH Eh	1.04	0.001	2.59	0.0003	2.93	0.0003
Plasma Cys ^b	-0.04	0.01	-0.06	0.14	-0.08	0.05
Plasma CySS	-1.38	< 0.0001	-2.57	0.0008	-2.66	0.002
Plasma Cys:CySS ^b	-0.17	0.30	-0.007	0.85	-0.03	0.42
Plasma Cys Eh	0.77	0.065	0.83	0.40	1.48	0.17

a – adjusted for age, sex, tv ownership, smoking (ever/never), log body mass index, log plasma folate
b – log transformed

Arsenic exposure was associated with significantly decreased concentrations of whole blood GSH, plasma Cys and plasma CYSS . Also, the positive association between As exposure and both blood GSH Eh and plasma Cys Eh, suggests that As exposure is associated with a more oxidizing redox state in both blood and plasma. However, As was not found to be associated with increased concentrations of other, possibly less sensitive, markers of oxidative stress, including plasma malondialdehyde and protein carbonyls (data not shown). Thus, these findings are most consistent with the hypothesis that As influences concentrations of non-protein sulfhydryls through binding and irreversible loss in urine and/or bile. Collectively, these results in humans demonstrate that As exposure depletes GSH, the body's most important defense against oxidative stress.

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Progress Report:

Project 1: *Genotoxic and Cell Signaling Pathways of Arsenic in Mammalian Cells*

PI: Tom Hei

1) The overall goals of this project remain unchanged.

2) During the current funding period, we examined the profile of pathway-specific phosphoproteins induced by arsenic in human cells. Human telomerase-immortalized human small airway epithelial cells (h-TERT SAEC) exposed to arsenite were used to identify phosphoproteins of two major signaling cascades, including the human phospho-receptor tyrosine kinase (Phospho-RTK) and the mitogen-activated protein kinases (MAPKs), which play an essential role in modulating genotoxic response of mammalian cells to arsenic. In arsenite-treated cells, phosphorylation of epidermal growth factor receptor (EGFR), InsulinR and Flt3R was significantly increased when compared to untreated controls. Inhibitors of these proteins further confirmed the involvement of these proteins in the neoplastic transformation of arsenite-treated human small airway epithelial cells as evidenced by changes in plating efficiency, anchorage-independent growth and proliferation rate. Our data provide further evidence that analysis of phosphoprotein induction can be very useful in understanding the carcinogenic mechanism of sodium arsenite.

In mammalian cells, genomic instability is considered a predisposition factor for cancer. To determine whether arsenic induces genomic instability and how the effect correlates with the exposure conditions, h-TERT SAECs were treated with inorganic arsenic at different doses and for various treatment periods. Treated and non treated control cells were analyzed for micronuclei formation, which was used as a surrogate marker for genomic instability. At a concentration of 1.4 μ M, a two-month treatment resulted in a micronucleus incidence that was twice the basal level. The incidence further increased such that after 14 months exposure, the micronucleus incidence was 7 fold higher than the controls. These data show that arsenic is genotoxic and induces genomic instability among treated cells.

In addition, to provide mechanistic insights on the role of the neurotoxicity of arsenic, we treated rat neuron-like PC12 cells with arsenite. We observed arsenite-induced apoptosis in both cancer (melanoma) cells and neuron-like PC12 cells 48 h after treatment with 2-4 μ M arsenite. Both melanoma cells and PC12 cells were characterized by surface expression of neuron growth factor-receptor (NGF-R). However, NGF (ligand) added to the cell media suppressed arsenite-induced apoptosis only in neuron-like PC12 cells via induction of the PI3K-

AKT pathway, but not in arsenate-sensitive melanoma cells. This differential response to a combination of arsenite and NGF will allow the protection of neurons from cytotoxic effects of arsenite, which has been used as a therapeutic regimen in cancer therapy.

3) Arsenic is an important environmental carcinogen that affects millions of people worldwide through contaminated water supplies. A better understanding of the mutagenic/carcinogenic mechanism of arsenic should provide a basis for better interventional approach in both treatment and prevention of arsenic induced cancer.

4) In the current funding period, we are not able to assess genomic instability in blood lymphocytes using the Bangladeshi cohort samples since all collected samples were pre-fixed in paraformaldehyde. In the coming year, we will resume our studies on mitochondrial DNA mutations in arsenic-induced skin lesions with or without concurrent UV exposure based on the Bangladeshi cohort.

Publications:

Ivanov, V.N., Partridge, M.A., Huang, S. X., and **Hei, T. K.** Suppression of the pro-inflammatory response of metastatic melanoma cells increased TRAIL-induced apoptosis. *J. Cell Biochem.* 2010. Nov. 15th. [Epub ahead of print] PMID: 21080331.

Wen, G.Y., Hong, M., Calaf, G. M., Roy, D., Partridge, M.A., Li, B., and **Hei, T.K.** Phosphoproteomic profiling of arsenite-treated human small airway epithelial cells. *Oncology Report* **23**: 405-412, 2010. PMID 20043101.

Karasic, T.B., **Hei, T.K.**, and Ivanov, V.N. Disruption of IGF-1R signaling increases TRAIL-induced apoptosis: a new potential therapy for the treatment of melanoma. *Experimental Cell Research* **316**:1994-2007, 2010. PMID 20417200

Students and Post-docs whose research is supported completely or in part by Project 1:

Gengyun Wen, PhD, was a post-doctoral fellow in Dr. Hei's lab during the past year.

Sarah X. Huang completed her PhD in Environmental Health Sciences under Dr. Hei's guidance.

Project 2: A Cohort Study of Health Effects of Arsenic Exposure in Bangladesh **PI: Habibul Ahsan**

This prospective cohort study recruited 11,746 men and women in Araihasar, Bangladesh, during 2000-2002 to investigate the health effects of arsenic exposure, with an initial focus on skin lesions and skin cancers. Between 2006 and 2008, the cohort was expanded to 20,033 individuals. Expansion participants were enrolled into the cohort through in-person interviews and had blood and urine samples collected in the same manner as the original cohort. The design of this multidisciplinary project and cohort description has been published (Ahsan et al., 2005). 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, and respiratory disease with the prospective data.

In-person interviews and clinical examinations of the cohort participants are conducted every 2 years. The eight-year follow-up visit of the original cohort and 4-year follow-up visit of the expansion cohort is currently underway using the same study instrument. To date, we have completed laboratory measurement of urinary total arsenic concentration in all baseline, two-year follow-up, and four-year follow-up samples from the original HEALS cohort and all baseline and two-year follow-up samples of the expansion cohort.

Utilizing the data collected from the first three follow-up visits (2-, 4-, and 6-year visits) of the original cohort, our prospective analyses based on individual-level data clearly suggest *increased mortality in relation to increases in arsenic exposure* based on water and urinary arsenic. These findings were recently published (Argos et al. Lancet 2010). We also have a manuscript under review, in which we observed an increased risk of cardiovascular disease mortality in relation to increases in arsenic exposure (Chen et al. Under review). Additionally, we utilized the prospective data through 6-years of follow-up to assess skin lesion incidence and observed a clear dose-dependent association between arsenic exposure and skin lesion risk, even at low exposure levels (water arsenic concentration <100 µg/L). This manuscript has been submitted for publication and currently being revised (Argos et al. Under review). Additionally, we have two publications in press reporting modification of the association between arsenic exposure and incident skin lesion status by smoking status in men (Melkonian et al. In press) and dietary patterns (Pierce et al. In press).

The objectives of our current analyses and follow-up interviews are to specifically examine the original aims which have not been modified since the last progress report. Several other manuscripts are being drafted for publication reporting results of our prospective cohort analyses of modification of the effects of arsenic on mortality and incidence of skin lesions.

In addition to the above-mentioned components, resources from this prospective cohort study have also yielded many other ancillary studies and publications including three additional R01 grants from NIH to investigate the genetic and nutritional aspects as well as chemoprevention of arsenic health effects.

Project 2 - Supported Publications:

Argos M, Kalra T, Rathouz PJ, Chen Y, Pierce B, Parvez F, Islam T, Ahmed A, Rakibuz-Zaman M, Hasan R, Sarwar G, Slavkovich V, van Geen A, Graziano J, Ahsan H. Arsenic exposure from drinking water, and all-cause and chronic-disease mortalities in Bangladesh (HEALS): a prospective cohort study. Lancet. 2010; 376(9737) :252-8. PMID: 20646756.

Argos M, Rathouz PJ, Pierce BL, Kalra T, Parvez F, Slavkovich V, Ahmed A, Chen Y, Ahsan H. Dietary B vitamin intakes and urinary total arsenic concentration in the Health Effects of Arsenic Longitudinal Study (HEALS) cohort, Bangladesh. Eur J Nutr. 2010. PMID: 20386915.

Chen Y, Ahsan H, Slavkovich V, Peltier GL, Gluskin RT, Parvez F, Liu X, Graziano JH. No association between arsenic exposure from drinking water and diabetes mellitus: a cross-sectional study in Bangladesh. Environ Health Perspect. 2010; 118(9): 1299-305. PMID: 20813654.

Melkonian S, Argos M, Pierce BL, Chen Y, Islam T, Ahmed A, Syed EH, Parvez F, Graziano J, Rathouz PJ, Ahsan H. A Prospective Study of the Synergistic Effects of Arsenic Exposure and Smoking, Sun Exposure, Fertilizer Use, and Pesticide Use on Risk of Premalignant Skin Lesions in Bangladeshi Men. American Journal of Epidemiology 2010; In press. PMID: 21098630.

Parvez F, Chen Y, Brandt-Rauf PW, Slavkovich V, Islam T, Ahmed A, Argos M, Hassan R, Yunus M, Haque SE, Balac O, Graziano JH, Ahsan H. A prospective study of respiratory symptoms associated with chronic arsenic exposure in Bangladesh: findings from the Health Effects of Arsenic Longitudinal Study (HEALS). *Thorax*. 2010; 65(6):528-33. PMID: 20522851.

Pierce BL, Kalra T, Argos M, Parvez F, Chen Y, Islam T, Ahmed A, Hasan R, Rakibuz-Zaman M, Graziano J, Rathouz PJ, Ahsan H. A prospective study of body mass index and mortality in Bangladesh. *Int J Epidemiol*. 2010; 39(4): 1037-45. PMID: 20032266.

Pierce BL, Argos M, Chen Y, Melkonian S, Parvez F, Islam T, Ahmed A, Hasan R, Rathouz PJ, Ahsan H. Arsenic exposure, dietary patterns, and skin lesion risk in Bangladesh: A prospective study. *American Journal of Epidemiology* 2010; In press.

Submitted Manuscripts:

Argos M, Kalra T, Rathouz PJ, Chen Y, Pierce B, Islam T, Ahmed A, Hassan R, Parvez F, Graziano J, Ahsan H. A Prospective Study of Arsenic Exposure from Drinking Water and Incidence of Skin Lesions in Bangladesh. Under Review (2010).

Chen Y, Graziano JH, Gamble MV, Liu M, Slavkovich V, Ahsan H. Arsenic exposure and cardiovascular mortality: a prospective cohort study. Under Review (2010).

Students and Post-docs whose research is supported completely or in part by Project 1:

Stephanie Melkonian, MPH, a current doctoral student at the University of Chicago

Maria Argos, MPH, a current doctoral student at Columbia University

Faruque Parvez, MPH, a current doctoral study at Columbia University

Gene Pesola, MD, MPH, post-doctoral fellow

Brandon Pierce, PhD, post-doctoral fellow

Project 3: *Consequences of Arsenic and Manganese Exposure on Childhood Intelligence*

PI: Joseph Graziano

This project builds upon our discovery that arsenic (As) and manganese (Mn) exposure from drinking water have adverse effects on intelligence in children. Two studies, in Bangladesh and New England, are in progress. Four years ago we launched a study of elementary school children in New Hampshire (NH) to determine whether exposure to As impairs intellectual functioning in a U.S. population. Because recruitment in NH was not proceeding at a sufficient rate, we expanded our study into Maine (ME) where recruitment is excellent and As exposure is more prevalent. To date, 307 children have been recruited and completed the protocol. Of these, 150 have been recruited in the past year, thanks to an Administrative Supplement that enabled us to hire a new staff member in ME.

Of the 250 children in the interim analysis, 80 had water As levels greater than the EPA standard of 10 ppb. Child IQ scores range from 81-147. Thus far, the mean IQ of those with water As < 10 ppb is 109.2 while the mean for those with water As > 10 ppb is 105.5. These very preliminary analyses are not conclusive, as we must still employ appropriate regression modeling to control for covariates.

The second portion of this project takes place in Bangladesh, where our research seeks to determine whether exposure to As and Mn has an adverse effect on motor function and on intelligence. This study involves a 2 x 2 design, i.e., high/low (<10 ppb) drinking water As and high/low (< 400 ppb) water Mn, with 75 children in each cell. Thus, half of the children in the study are drinking water with As and Mn levels below the WHO guideline. We completed the recruitment of all 300 children, 7-9 years of age. Our first publication, submitted, relates to child intelligence: When adjusted only for each other, both As and Mn in blood (BAs; BMn) were significantly negatively related to most WISC-IV subscale scores. With further adjustment for socio-demographic features and ferritin, BMn remained significantly associated with reduced Perceptual Reasoning and Working Memory scores; associations for BAs, and for other subscales, were expectably negative, but largely non-significant. Urinary As (per gram creatinine) was significantly negatively associated with Verbal Comprehension scores, even with adjustment for BMn and other contributors. Mn by As interactions were not significant in adjusted or unadjusted models.

A second submitted manuscript describes a novel finding, i.e., that BMn (but not BAs) is adversely associated with child behavior. Using the Child Behavior Checklist, Teacher's Report Form, we observed that water manganese (WMn) was positively and significantly associated with TRF internalizing, externalizing and total TRF scores in models adjusted for WAs and sociodemographic covariates. We also observed a dose-response relationship between WMn and TRF externalizing and TRF total scores among the participants of the study. We did not find any associations between WAs and various scales of TRF scores. These observations reinforce the growing concern regarding the neurotoxicologic effects of WMn in children

A third manuscript that is nearly completed, is described in Highlight #1 above. In short, BAs (but not BMn) is adversely associated with motor function in these same 300 children.

The next phase of the Bangladesh work involves remediation of the ongoing As and Mn exposures via the installation of deep tube wells in each child's village by our earth science investigators (Project #7). We will reassess motor function and intelligence over time to determine whether the consequences of exposure are reversible. The installation of deep wells low in As and Mn has been completed (see Project #7).

Student Involvement:

Christine George, Dr. Graziano's PhD student, is currently spending one year in Bangladesh with support of a Fulbright scholarship. She will defend her PhD dissertation during the coming year.

Lauden Behrouz derived her MPH dissertation in Epidemiology from this project.

Khalid Khan, completed his DrPH degree in EHS, and was responsible for the assessment of child behavior, and the development of a classroom based arsenic education program.

Faruque Parvez, who conducted the studies of motor function, will complete his DrPH degree in the coming year.

Project 3-Supported Publications:

There have been no publications from project #3 during the past year, though the PI has been a co-author of seven other publications derived from projects #2 and #4. This is due to the fact that we have been conducting field work throughout the year. Two manuscripts are in review, and a third is about to be submitted:

Wasserman, G, Liu, X, Parvez, F, Factor-Litvak, P, Ahsan, H, Levy, D, Kline, J, van Geen, A, Mey, J, Slavkovich, V, Siddique, A, Islam, T, Graziano, J: Arsenic and manganese exposure and children's intellectual function. Submitted

Khan, K, Factor-Litvak, P, Wasserman, GA, Liu, X, Ahmed, E, Siddique, A, Islam, T, Parvez, F, Slavkovich, V, Levy, D, Mey, J, van Geen, A, Graziano, J: Effect of water-borne manganese exposure from drinking water on children's classroom behavior in Bangladesh. Submitted

Parvez, F, Factor-Litvak, P, Wasserman, GA, Liu, X, Siddique, A, Islam, T, Parvez, F, Slavkovich, V, Levy, D, Mey, J, van Geen, A, Graziano, J: Effect of water-borne arsenic exposure on motor function in children in Bangladesh. Near submission.

Project 4: *One-Carbon Metabolism, Oxidative Stress and Arsenic Toxicity in Bangladesh*

PI: Mary V. Gamble

Nutritional status may account for some of the considerable variability in progression from arsenic (As) exposure to manifestations of disease. Methylation of ingested inorganic As (InAs) to methylarsonic- (MMA) and dimethylarsinic acids (DMA) relies on folate-dependent one carbon metabolism and facilitates urinary As elimination. Our SBRP project builds upon our Nutritional Influences on As Toxicity (NIAT) studies which demonstrated that folic acid supplementation increases As methylation and lowers blood As and blood MMA concentrations.

The first aim utilized the repository of biological samples (from Project #2) to conduct a nested case-control study. We tested the hypothesis that at the time of enrollment, participants who subsequently developed As-induced skin lesions (SLs) had lower folate and/or higher homocysteine as compared to non-skin lesion controls; we also analyzed genomic methylation of leukocyte DNA. The odds ratios (95% C.I.s) for subsequent development of SLs for participants who had low folate, high Hcys, or hypomethylated PBL-DNA were 1.6 (1.05 – 2.5; $p = 0.005$), 1.7 (1.1 - 2.6; $p = 0.01$), and 1.7 (1.1 – 2.7; $p = 0.008$), respectively, indicating that folate deficiency, hyperhomocysteinemia, and hypomethylation of genomic DNA are risk factors for As-induced skin lesions (Pilsner et al, EHP, 2009).

We also proposed to analyze biomarkers of oxidative stress. Analyses of urinary 8-oxo-2'-deoxyguanosine suggest that this biomarker is not associated with risk for skin lesions. Additional biomarkers were to include malondialdehyde (MDA) and protein carbonyls. However, our results from aim 3 (a dose-response study are arsenic-induced oxidative stress), we did not find arsenic exposure to be associated with increased MDA. We therefore made an executive decision not to waste precious biological samples and funds to repeat the analysis of MDA for this aim.

For the second aim, we proposed to examine the extent to which urinary As metabolites reflect As metabolites in blood in Bangladeshi adults. The Spearman correlations between As

in blood and urine ranged from 0.68 to 0.81 ($p < 0.0001$ for all metabolites). However, when expressed as a percentage of total As, the correlations were less strong (0.32 – 0.44; $p < 0.001$). Most striking were the differences in %MMA (13% in urine vs. 40% in blood) and %DMA (72% in urine vs. 34% in blood), consistent with a short circulating half-life of DMA which is rapidly excreted in urine (Gamble et al, AJCN, 2007).

For the dose-response study of the third aim, 375 participants were enrolled, and biological samples have been analyzed for reduced and oxidized glutathione, reduced and oxidized cysteine, MDA and protein carbonyls. Our analyses suggest that As exposure is associated with decreased concentrations of reduced glutathione (GSH) in whole blood and reduced concentrations of both reduced and oxidized cysteine in plasma, consistent with the hypothesis that As exposure is associated with depletion of glutathione. Since GSH is the body's primary antioxidant, this would be expected to be associated with increased oxidative stress. However, arsenic exposure is not significantly associated with other markers of oxidative stress including oxidized GSH, oxidized cysteine, plasma MDA or protein carbonyls. The final measure of oxidative stress currently being evaluated for this aim is urinary 8-oxodG.

Publications during the past year:

Hall MN, Liu X, Slavkovich V, Ilievski V, Mi Z, Alam S, Factor-Litvak P, Ahsan H, Graziano JH, and Gamble MV. Influence of Cobalamin on Arsenic Metabolism in Bangladesh, *Environ Health Perspect*, 2009;117(11):1724-9.

Pilsner JR, Hall MN, Liu X, Ahsan H, Ilievski V, Slavkovich V, Levy D, Factor-Litvak P, Graziano JH, Gamble MV. Associations of Plasma Selenium with Arsenic and Genomic Methylation of Leukocyte DNA in Bangladesh. *EHP* (in press).

Hall M, Niedzwiecki M, Alam S, Liu X, Oka J, Slavkovich V, Ilievski V, Levy D, Siddique A, Parvez F, Graziano JH and Gamble MV. Association between chronic arsenic exposure and blood glutathione concentrations in Bangladesh. (manuscript in preparation)

Pilsner JR, Liu X, Hall M, Rahman M, Factor-Litvak P, Graziano JH, and Gamble MV. Influence of maternal arsenic exposure on genomic DNA methylation in maternal-newborn pairs. (manuscript in preparation).

Harper K, Khan K, Hall M, Liu X, Graziano JH and Gamble MV. Arsenic exposure is not associated with urinary 8oxodG or risk for arsenic-induced skin lesions in Bangladesh (manuscript in preparation).

Pilsner JR, Liu X, Ahsan H, Ilievski V, Slavkovich V, Levy D, Factor-Litvak P, Graziano JH, Gamble MV. Influence of folic acid supplementation on DNA methylation in Bangladeshi adults. (manuscript in preparation).

Hall M, Neugut D, Pilsner JR, Liu X, and Gamble MV. Influence of arsenic exposure on plasma cystatin C, a sensitive marker of renal function. (manuscript in preparation).

Cappelli C, Barr D, Liu X, Graziano JH and Gamble MV. Differences in heavy metal concentrations between males and females, following adjustment for creatinine.

Students and Post-docs whose research is supported completely or in part by Project 4:

Megan Niedzwiecki, a current PhD student in Environmental Health Sciences

Megan Hall, PhD, a post-doctoral fellow who recently received a K99-R00 as a result of her work.

Larissa Calancie,BS, who was initially supported for a summer with ARRA funding, then stayed on to work for a year; now applying to PhD programs

Kristin Harper, PhD, a post-doctoral fellow supported by the Mellon Foundation

Project 5: *Mobilization of Natural Arsenic in Groundwater*

PI: Alexander van Geen

Co-Investigators: Yan Zheng, Martin Stute

In 2010 we focused on 2 themes: (1) Arsenic adsorption and its implication for transport of arsenic in shallow aquifers of Bangladesh, (2) processes regulating As levels in groundwater in Maine.

Kinetics and Equilibrium of As mobilization in Bangladesh

Kathleen Radloff conducted a study along a flow path that leads from a sandy recharge area in a village where groundwater As levels are as low as 10 µg/L to a nearby stream where As concentrations exceed 500 µg/L. She documented that the distribution coefficient for As describing the partitioning of As between the sands and groundwater was remarkably constant (~2 L/kg) along the transect despite relatively constant As levels released from the solid phase by a 1 M phosphate extraction. Arsenic speciation data obtained by X-ray absorption spectroscopy suggests that the discrepancy may reflect the precipitation of As-sulfides that contribute to keeping groundwater As levels low in the recharge area (Aziz et al., 2010a). Subsequent column experiments supported this interpretation.

³H-³He dating of the samples along the same transect in Bangladesh indicates a broad increase in As concentrations with groundwater age that is consistent with results previously reported by our team from elsewhere in Araihasar. This relationship can be reproduced by a simple groundwater flow and As transport model constrained by the new data from the site. The key implication is that there is significant As adsorption even in aquifers composed of reduced (grey) sands of Bangladesh which means that changes in As concentrations will be retarded by at least a factor of ten due to a large pool of exchangeable As present in the solid phase (Aziz et al., 2010b).

Arsenic During Groundwater Discharge

During groundwater discharge along the Meghna River in Bangladesh and at Waquoit Bay, MA, the partitioning of As between groundwater and sediment is also controlled by sorptive equilibrium. High spatial density piezometers show that groundwater Fe and As showed systematic attenuation from well water to riverbank or bayside porewater, indicating trapping of As in a reactive barrier consisting of amorphous Fe-oxides (Jung and Zheng, submitted-a; Jung et al., submitted-b).

Bedrock Geology and Arsenic Distribution in Greater Augusta, Maine

A geostatistical analysis demonstrates that the bedrock geology controls the spatial pattern of As distribution at intermediate scale (1-10 km) in the study area in Maine. A logistic regression model showed that bedrock geology, soil arsenic content, groundwater pH, dissolved oxygen, nitrate and sulfate played important roles in controlling groundwater arsenic concentrations. The logistic regression model was verified by additional sampling in 2010 of well water (n=307) in 5 additional towns where 23% of wells were found to contain arsenic greater than 10 µg/L. New results confirm a strong spatial association between groundwater arsenic and bedrock geology, pH, dissolved oxygen and nitrate concentrations. This detailed hydrogeochemical study has focused our attention on three wells to illustrate the effects of different flow paths on As concentrations in fractures using geophysical logging combined with fracture-specific water sampling in 2010.

Students and Post-docs whose research is supported completely or in part by Project 5:

Bethany O'Shea, Post-doc fellow, Columbia University Science Fellow. Currently Assistant Professor, San Diego State University

Hun Bok Jung, Ph.D., 2009, Earth and Environmental Sciences, City University of New York (CUNY). Currently post-doctoral research scientist at University of Wisconsin-Madison.

Kathleen A Radloff, Ph.D. 2010, Earth and Environmental Engineering, Columbia. Currently post-doctoral research scientist at Lamont-Doherty

Qiang Yang, Ph.D. 2010, Earth and Environmental Sciences, CUNY. Currently post-doctoral research scientist at Lamont-Doherty

Ivan Mihajlov, 3rd yr PhD student, Earth and Environmental Sciences, Columbia University

Ashley MacLean, Undergraduate, Columbia College

Margaret Bounds, Undergraduate, Environmental Science, Barnard College

Stephen Barten, Undergraduate, Environmental Science, Columbia College

Hosea Siu, Intel-Westinghouse Semi-Finalist, Bronx High School of Sciences. Currently undergraduate student at MIT

Project 5-Supported 2010 Publications:

Aziz, Z., B. Bostick, Y. Zheng, M.R Huq, M.M. Rahman, K.M. Ahmed, and A. van Geen (submitted), Suppression of arsenic release to shallow groundwater of Bangladesh by reduced sulfur, resubmitted to *Environmental Science and Technology*, October 2010a

Aziz, Z, M. Stute, R. Versteeg, P. Schlosser, MR Huq, KM Ahmed, A van Geen, Distribution of As in shallow Bangladesh aquifers of Bangladesh controlled by desorption and flushing: An evaluation at the village-scale using a 3-D groundwater flow model, submitted to *Water Resources Research*, November 2010b.

Dhar, R.K., Y. Zheng, C.W. Saltikov, K. A. Radloff, B. Mailloux and A. van Geen (submitted). Microbes Enhance Mobility of Arsenic in Pleistocene Aquifer Sand from Bangladesh. Revised and submitted to *Environmental Science and Technology*, September 2010

Garnier, J.-M., F. Travassac, V. Lenoble, J. Rose, Y. Zheng, M. Hossain, S. Chowdhury, A. Biswas, K.M. Ahmed; Z. Cheng, A. van Geen, Temporal variations in arsenic uptake by rice plants: The role of iron plaque in paddy fields of Bangladesh irrigated with groundwater, *Science of the Total Environment*, **408**, 4185-4193, 2010.

He Y. and Zheng Y. (2010) Assessment of in vivo bioaccessibility of arsenic in dietary rice by a mass balance approach. *Science of the Total Environment*. **408**, 1430-1436

Jung H. B. and Zheng Y. (submitted-a) Fate of Arsenic during Groundwater Discharge to Meghna River in Bangladesh. *Geochimica Cosmochimica Acta*.

Jung H. B., Zheng Y., Bostick B., Datta S., Rahman M. W., Rahman M. M., and Ahmed K. M. (submitted-b) Chemical Fluxes Regulated by Hyporheic Zone Reactions during Groundwater Discharge in the Ganges-Brahmaputra-Meghna Delta. *Geochimica Cosmochimica Acta*.

Mladenov N, Zheng Y, Miller MP, Nemergut DR, Legg T, Simone B, Hageman C, Rahman MM, Ahmed KM, McKnight DM, Dissolved organic matter sources and consequences for iron and arsenic mobilization in Bangladesh aquifers, *Environmental Science and Technology*, **44**, 123-128, 2010

Wagner PJ, R Foster, JF Stolz, MB Scholz, K Wovkulich, GA Freyer, A van Geen, SN Chillrud, Y Zheng, KM Ahmed, BJ Mailloux, Worldwide diversity and occurrence of arsenite transporter *acr3(2)* suggests an important and overlooked pathway for arsenate reduction, submitted to *Environment Microbiology Reports*, May 2010.

Zheng, Y. (2010) Flushing of arsenic from aquifer: Implications for safe drinking water options in high arsenic occurrence areas. In J.-S. Jean, J. Bundschuh, and P. Bhattacharya (ed.) *Arsenic in Geosphere and Human Diseases: As2010*. CRC Press, Taylor & Francis Group, Leiden, the Netherlands, pp.90-93

Progress Report Project 6: *Mobilization of anthropogenic arsenic in groundwater*
PIs: Steven Chillrud, Martin Stute, Brian Mailloux

Project 6 investigates the geochemistry and remediation of arsenic associated with the Vineland Superfund site in southern New Jersey. This involves work on the site of a former arsenic herbicide manufacturing facility as well as downstream at a recreational lake impacted by site arsenic. Due to decades of improper chemical storage and disposal by Vineland Chemical, the site was extensively contaminated with arsenic. Despite nearly a decade of pump-and-treat remediation, groundwater arsenic concentrations can still be several hundred µg/L. Laboratory column experiments using contaminated Vineland aquifer solids have suggested that current aquifer clean-up strategies, relying on pump-and-treat to flush groundwater through the aquifer, could require hundreds of years but the remediation timeframe could be decreased substantially (to <5 years) by introducing oxalic acid to the system. We have also conducted a pilot experiment where we injected oxalic acid and tracers into a very small portion (~50 m²) of the aquifer next to one of the large volume extraction wells. Approximately 3 kg of arsenic was successfully removed by the oxalic acid, similar in magnitude

to the amount of solid phase arsenic within the small pilot area. Overall, our work suggests that addition of oxalic acid shows promise for accelerating treatment of a highly contaminated site offering the potential to lower dramatically the As remediation time-scale.

Our activities over the last year have focused on additional laboratory measurements and experiments on samples from the Vineland Site, data analysis and manuscript preparations, and a series of meetings with the Vineland Site Managers (EPA Region 2 and USACE) to plan future activities at the Vineland Site. We have been completing the analyses of samples collected as part of the spring/summer 2009 pilot experiment and samples collected from Union Lake. We have also developed a new method to integrate the use of microfocused synchrotron techniques with column transport experiments to simultaneously monitor grain-scale solid phase reactions and column scale transport in order to better understand As release and transport processes. Small column experiments (~4 cm long x 0.635 cm ID) were performed on the laboratory bench as well as in the synchrotron beamline. Microfocused synchrotron X-ray fluorescence (μ SXRF) maps for As and Fe were collected at the same location in the columns (<1 mm²) before and during treatment with 10 mM oxalic acid. Based on μ SXRF counts, between 79% and 83% of As was removed from the sediments by the oxalic acid treatment; these removal percentages agreed well with laboratory data based on integrating column effluent (88-95%). A smaller percentage of Fe was removed, 14-25% based on μ SXRF counts; column effluent indicated 7-9% Fe removal. A combination of laboratory columns, μ SXRF data, and geochemical models were used to investigate As release rates during oxalic acid treatment. A pore volume based As removal rate was used to create a PHREEQC 1-D transport model, which indicated that microscale processes can be predictive of the larger system.

Students and Postdocs involved in studies in 2010:

Karen Wovkulich, Ph.D. student, Earth and Environmental Science, Columbia University

Kamini Doobay, undergraduate, Environmental Sciences, Barnard College

Hannah Perls, undergraduate, Environmental and Earth Sciences, Columbia University

Jennie Harkness, undergraduate, Chemistry, Vassar College

Heili Lowman, undergraduate, Chemistry, Vassar College

Governmental agency staff we interact with on Vineland Superfund Site:

Ron Naman, John Frisko and Nica Klaber from EPA Region 2; Steve Creighton and Laura Bittner from USACE-Philadelphia; Craig Wallace and Chad Vansciver from NJDEP

2010 publications and meetings:

Wovkulich, K., Mailloux, B. J., Lacko, A., Keimowitz, A. R., Stute, M., Simpson, H. J., Chillrud, S.N., 2010. Chemical Treatments for Mobilizing Arsenic from Contaminated Aquifer Solids to Accelerate Remediation. *Applied Geochemistry*, 25: 1500–1509. PMID: PMC2976553. doi:10.1016/j.apgeochem.2010.08.001

Wovkulich, K., M. Stute, T.J. Protus Sr., B.J. Mailloux, S.N. Chillrud. Injection System for Multi-Well Injection Using a Single Pump. *Ground Water Monitoring and Remediation.*, in press, Dec 2010.

Chillrud, S.N., M. Stute, K. Wovkulich. Working Together: Getting the Best Results Through Partnerships (Everybody Wins!). National Association of Remedial Project Managers, May 24-27, 2010. Crystal City, VA.

Project 7: Mitigation of Arsenic Mobilization in Groundwater

PI: Alexander van Geen

Co-Investigators: Yan Zheng, Martin Stute.

Research carried out under this project in 2010 focused on 3 themes: (1) deep aquifers of Bangladesh as sources of low-As drinking water, (2) the protection of shallow low-As aquifers more generally by adsorption, and (3) training and education at the village and school level in Bangladesh to reduce As exposure. These activities have resulted this year in 5 published papers and 6 submissions.

The NGO Water Aid, Bangladesh, installed 60 deep (700-800 ft) community wells serving the needs of our cohort of 20,000 men and women living in the study area of Araihasar. The water from all but one of these wells, which needs to be re-installed, now provides thousands of villagers with drinking water that meets the WHO guideline for As in drinking water of 10 µg/L. As a result, we expect to record a major reduction in the urinary As levels measured under Core B and significant improvements in health over the long-term that will be quantified under the cohort study (Project 2) and the children's study (Project 3). As a service to the Government of Bangladesh, which has already installed ~100,000 deep wells throughout the country, Proj. 7 is initiating the sampling of a subset of 3000 deep wells distributed across the vulnerable portions of the country. In turn, this will provide us with a rich dataset for future investigations. A first batch of 150 samples collected with financial support from the Dhaka office of WHO was analyzed under Core C for As, Mn and other elements of potential health concern. The survey has identified two regions where even deep aquifers are systematically elevated in As, but very few well failures in other regions.

Kathleen Radloff, supported in part by Proj 7, has defended her PhD and is preparing three manuscripts for publication, one of which documents how As adsorption protects deeper aquifers against intrusion of shallow contaminated groundwater. PhD student Ivan Mihajlov has conducted some elegant column experiments in the field supporting these results. Dr. Holly Michael of the University of Delaware has new data to predict the vulnerability of deep aquifers of Bangladesh in the coming decades using a regional groundwater flow model. Zahid Aziz has also defended his PhD and submitted two manuscripts focused on processes regulating As concentrations in shallow aquifers.

Project 7 continues to be involved in the field research of two graduate students at the Mailman School of Public Health. Christine George, supported in part by a Fulbright fellowship, is about to complete a randomized controlled trial in two dozen villages in Bangladesh. Her intervention was designed to compare the impact on household behavior of field-kit testing wells for As by an outsider or a resident of the village. Khalid Khan, supported primarily through the Fogarty training grant, defended his PhD and will continue to analyze as a post-doc the results from a randomized controlled trial designed to determine whether school-level education amplifies the reduced exposure of children anticipated from the recent installation of deep community wells in Araihasar.

Manuscripts published or in press (5) and submitted (6) in 2010

Fendorf S., H. Michael, A. van Geen, Spatial and temporal variations of groundwater arsenic in South and Southeast Asia, *Science*, 328, 1123-1127, 2010.

Argos, M., T Kalra, PJ Rathouz, Y Chen, B Pierce, F Parvez, T Islam, A Ahmed, M Rakibuz-Zaman, R Hasan, G Sarwar, V Slavkovich, A van Geen, J Graziano, H Ahsan, A prospective cohort study of arsenic exposure from drinking water and all-cause and chronic disease mortality in Bangladesh, *The Lancet*, DOI:10.1016/S0140-6736(10)60481-3, 2010.

Garnier, J.-M., F. Travassac, V. Lenoble, J. Rose, Y. Zheng, M. Hossain, S. Chowdhury, A. Biswas, K.M. Ahmed; Z. Cheng, A. van Geen, Temporal variations in arsenic uptake by rice plants: The role of iron plaque in paddy fields of Bangladesh irrigated with groundwater, *Science of the Total Environment*, 408, 4185-4193, 2010.

Leber J, MM Rahman, KM Ahmed, B Mailloux, A van Geen, Contrasting influence of geology on E. coli and arsenic in aquifers of Bangladesh, *Ground Water* doi: 10.1111/j.1745-6584.2010.00689.x, 2010.

Aziz, Z, M. Stute, R. Versteeg, P. Schlosser, MR Huq, KM Ahmed, A van Geen, Distribution of As in shallow Bangladesh aquifers of Bangladesh controlled by desorption and flushing: An evaluation at the village-scale using a 3-D groundwater flow model, submitted to *Water Resources Research*, November 2010.

Aziz, Z., B. Bostick, Y. Zheng, M.R Huq, M.M. Rahman, K.M. Ahmed, and A. van Geen, Suppression of arsenic release to shallow groundwater of Bangladesh by reduced sulfur, resubmitted to *Environmental Science and Technology*, October 2010.

Benear L, A Tarozzi, A Pfaff, HB Soumya, KM Ahmed, A van Geen, Bright lines, risk beliefs, and risk avoidance: Evidence from a randomized intervention in Bangladesh, submitted to *American Economic Journal: Applied Economics*, October 2010.

van Geen A, KM Ahmed, Y Akita, MJ Alam, PJ Culligan, J Feighery, A Ferguson, M Emch, V Escamilla, P Knappett, AC Layton, BJ Mailloux, LD McKay, JL Mey, ML Serre, PK Streatfield, J Wu, M Yunus, Fecal contamination of shallow tubewells in Bangladesh inversely related to arsenic, resubmitted to *Environmental Science and Technology*, September 2010.

Chen Y, JH Graziano, F Parvez, M Liu, V Slavkovich, T Kalra, M Argos, T Islam, A Ahmed, M Rakibuz-Zaman, R Hasan, D Levy, A van Geen, and H Ahsan, Arsenic exposure from drinking water and cardiovascular disease mortality: A prospective cohort study in Bangladesh, submitted to *British Medical Journal*, October 2010.

Wagner PJ, R Foster, JF Stolz, MB Scholz, K Wovkulich, GA Freyer, A van Geen, SN Chillrud, Y Zheng, KM Ahmed, BJ Mailloux, Worldwide diversity and occurrence of arsenite transporter *acr3(2)* suggests an important and overlooked pathway for arsenate reduction, submitted to *Environment Microbiology Reports*, May 2010.

Students supported at least in part under Project 7 in 2010

Kathleen Radloff, Earth & Environmental Engineering, Columbia, PhD June 2010.

Zahid Aziz, Earth & Environmental Sciences, Columbia, PhD December 2010.

Khalid Khan, Mailman School of Public Health, Columbia, PhD September 2010.

Ivan Mihajlov, Earth & Environmental Sciences, Columbia, PhD candidate.

Christine George, Mailman School of Public Health, Columbia, PhD candidate.

Misheal Artani, Environmental Sciences, Barnard College, Sr Undergraduate.

Pamela Mishkin, senior at Horace Mann High School

Administrative Core.

Director: Joseph Graziano
Deputy Director: Alexander van Geen

General Activities: The Administrative Core continues to function smoothly. Dr. Graziano, the Program Director, and Dr. van Geen, the Associate Director, have been working together with SRP investigators to plan for the upcoming competitive renewal application in April, 2011. The Director and Deputy Director have led weekly series of meeting among biomedical and non-biomedical scientists, respectively, to develop sets of research aims that would be most appropriate for support by the SRP Program. We communicate continuously with regard to the integration of our biomedical and non-biomedical research programs, and hold joint monthly meetings of all faculty to maximize the interactions across biomedical and non-biomedical projects. This communication is evidenced by the number of truly multi-disciplinary publications that have come from our program, involving close collaboration between biomedical, earth, and social scientists.

All of the scientific team has assembled 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. In the past year, many of these sessions have been devoted to discussions and planning for our competitive renewal application. Others have been devoted to two hours of seminars, typically one hour for biomedical and one for non-biomedical presentations. Seminars that have occurred in the past year include:

December 21st , 2009

"Arsenic exposure, cardiovascular disease mortality, and the potential effect-modifiers" presented by Dr. Yu Chen, NYU's School of Medicine

March 22nd, 2010

"Arsenical drugs in food animal production- where we should be, and how we'll get there" by Keeve E. Nachman, Science Director for Food Production, Health, and Environment at the Center for a Livable Future, Bloomberg School of Public Health, Johns Hopkins University

"Sources, transformations, and mobility of roxarsone in the environment: Implications to risk assessment" presented by Benjamin C. Bostick, Lamont-Doherty Earth Observatory, Columbia University

October 18, 2010

"The role of recharge in both flushing aquifers clean and mobilizing arsenic in Bangladesh" presented by Charles Harvey, Department of Civil Engineering, Massachusetts Institute of Technology

"Mechanistic Work on Mn Neurotoxicity in Non-human Primates" presented by Tomás R. Guilarte, Environmental Health Sciences, Mailman School of Public Health, Columbia University

December 6, 2010

"Immunotoxic Effects of Developmental Arsenic Exposure" presented by Courtney Kozul-Horvath, Department of Immunology, Dartmouth Medical School

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) Allan Smith, Professor of Epidemiology, University of California, Berkeley; f) X. Chris Le, Professor of Public Health Sciences, University of Alberta; and g) Peggy O'Day, Associate Professor of Natural Sciences, University of California, Merced. Given the thrust of our proposed work in the coming grant cycle, we have added one more committee member, i.e., Dr. Robert Wright, Associate Professor of Environmental Health Sciences and Pediatrics at Harvard. Dr. Wright is the PI of the Harvard SRP, and has expertise related to each of the four biomedical projects that will be presented in our renewal application.

The External Advisory Committee visited Columbia University twice during the past year, in April and November, 2010. At the April meeting, each of our seven research project PIs, as well as the PIs of the Research Translation Core, made presentations to the Committee and many research issues were discussed at length. At the recent November meeting, each of the PIs of the seven research projects presented a tentative set of Specific Aims and the justification and general approach to those aims. The meeting was enormously helpful in guiding our future work, and, since that meeting, several committee members (particularly Drs. Wright, Karagas and Szabo) have continued to provide new suggestions and the names of potential collaborators by e-mail and telephone.

In November, the SRP director, several PI's, the Business Manager, the RTC Core Leader and 4 students attended the annual SRP meeting.

Finally, this core is already deeply involved in the preparation of the April 15 application, with regard to budget allocations for each project and core.

Core A: *Data Management Core*

PI: Diane Levy

1. Project 2:
 - a. Customized data entry system in Bangladesh was used to complete 2 phases of data entry for HEALS:
 - i. Follow up 3 for 11,540 original participants
 - ii. Follow up 1 for 8,267 new participants (ACE)All data were periodically automatically transferred to Columbia University SQL database located in NY.
 - b. New data entry screens were programmed to duplicate the follow up 4 questionnaire to be administered to HEALS participants. The system has been tested by New York staff and will be installed for testing in Dhaka.
 - c. Data sets have been provided to project investigators as requested.
2. Project 3:
 - a. New Hampshire/Maine
 - i. Data for 256 children were entered. Data entry includes a demographic/well questionnaire, WISC and WASI tests, and a home assessment questionnaire
 - ii. Data sets are being assembled for interim analysis
 - b. Bangladesh
 - i. Scoring for manual dexterity testing was completed
 - ii. Datasets were updated and distributed for analysis.

3. Project 4:
 - a. Periodic uploads of laboratory data to Microsoft SQL server database. The following data have been added: plasma folate, B12, homocysteine, cysteine, Cystatin C; leukocyte DNA methylation; urinary 8-OHdG (8-hydroxydeoxyguanosine); serum retinol and carotenoids (including leutein/zeaxanthin (one variable); beta-cryptoxanthin, lycopene, alpha-carotene, and beta-carotene) serum tocopherol, arsenic (total and metabolites for both blood and urine), glutathione, glutathione disulfide, cysteine, cystine, global DNA methylation by [3H]-methyl incorporation assay, global DNA methylation by pyrosequencing (LUMA, Line-1, and Alu), plasma malondialdehyde. Protein carbonyl, s-adenosylmethionine (SAM) and s-adenosylhomocysteine (SAH) data will be added very soon.
 - b. Data sets have been distributed to PI and biostatistician for analyses
 - c. Collectively, data from Project 4 and ancillary studies have resulted in 20 publications (including 13 published and 7 in preparation).
4. Additional efforts:
 - a. Health Education of School Children in Bangladesh:
 - i. Consultation with PI for follow up questionnaire
 - ii. Database programming and dataset creation will follow
 - iii. Datasets were created for analyses
 - b. Community Participation Database
 - i. Consultations continued with PI re: questionnaire design, work flow and database
 - ii. Additional modules programmed:
 1. individual screening
 2. baseline questionnaire
 3. follow up questionnaire
 - iii. Ten percent of questionnaires checked by staff for determination of data entry error rates
 - c. Neurological Outcomes/Tremor Study (Elan Louis, PI)
 - i. Loaded neurological outcomes database into Arsenic project database
 - ii. Created process for entering spiral test results; results loaded in SQL database.
 - iii. Datasets distributed to PI and Xinhua Lui for analysis
 - d. Created/taught data management workshop for NIEHS and Superfund investigators, staff and students.
 - e. Continued support for undergraduate and graduate students working with PIs on Arsenic related projects.
 - f. Continued maintenance of secure database and web servers. Projects detailed above are direct beneficiaries of these services.
 - g. Management of data flow continues using the Issue Tracking System and the Query Tracking Systems.
 - h. Attending weekly project team meetings to provide data management consultation as projects move forward.

Core B: Trace Metals Core Laboratory

PI: Joseph Graziano

Laboratory Director: Vesna Slavkovich

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 #2, #3 and #4.

During the past year, this Core Lab conducted more than 30,000 “routine” analyses of biological samples from projects 2, 3 and 4. A main focus of the Core’s activities has been analytical support for As and creatinine measurements for the HEALS Cohort Study (Project #2), which is now in its fourth biannual follow-up visit. Roughly one half of the laboratories analyses have gone to support Dr. Mary Gamble’s studies of folate and creatine supplementation in the FACT Study (Folate and Creatine Trial; N = 800), as well as Dr. Ahsan’s BEST study (Bangladesh Vitamin E and Selenium Trial; N = 8000). In addition, in support of Dr. Gamble’s FOX study (Project #3: Folate, Arsenic and Oxidate Stress), 400 urinary, and blood measurements were conducted, including measurements of arsenic metabolites by HPLC-ICP-MS-DRC technology.

Given the similarities in the metabolism of Mn and Fe, we have also conducted various measurements related to Fe metabolism in various studies of children and adults. These have included hemoglobin, plasma iron, ferritin and transferrin receptors.

Four years ago, the Trace Metals Core developed a new method for the analysis of arsenic in blood, using ICP-MS-DRC. That method allowed us to demonstrate that blood As is an extremely useful biomarker of exposure. Moreover, the method allows for the simultaneous measurement of other metals of interest that are covariates in many analyses, namely Pb, Mn and Se. During the past year the lab has continued to provide these blood analyses to several projects, notably Project #4.

Given the potential utility of blood arsenic measurements in epidemiologic research, last year we validated the use of fingerstick blood samples for the analysis of As in blood. This method is now in full use, and has allowed for repeat measurements of blood As concentrations in Dr. Gamble’s large folate/creatine trial (i.e., the FACT Study). Approximately 2400 finger stick samples have been collected and are in the process of being analyzed by this new method.

Students involved with this work:

Christine George, Dr. Graziano’s minority Ph.D. student, who has a degree in Environmental Engineering from Stanford University. She has been awarded a Fulbright Award and will be returning to Columbia on 12/23/10 after spending one year in Bangladesh where she is currently working on her dissertation research project.

Khalid Kahn, Dr. Graziano’s Bangladeshi student completed his DrPH in October, 2010.

Jacqueline Factor-Litvak, a Tuft’s undergraduate, worked in the lab during the summer.

Seyed Zonoor, an undergraduate from UCSF, also worked in the lab during the summer and is now a full-time employee of the lab; he is applying to medical school now.

Tiffany Sanchez, a minority Columbia undergraduate, also worked in the lab during the summer and is now a full-time employee of the lab; she is applying to our PhD program in EHS.

Trace Metals Core-Supported Publications:

Every publication listed for Projects 2, 3 and 4 has relied on the Trace Metal Core.

Core C: *Biogeochemistry Core*

PIs: Alexander van Geen and Steven Chillrud

Co-investigators: Brian Mailloux and Benjamin Bostick, also Jacob Mey and James Ross.

The Biogeochemical analytical core laboratory is housed at Lamont-Doherty Earth Observatory (LDEO). It provides sample preparation and analyses to six projects of the Columbia Superfund program. Analyses have been carried out by high-resolution inductively coupled plasma mass spectrometry for up to 33 elements for water, soil, sediment, leachate, and plant material (HR ICP-MS). We have also recently acquired a polarized energy dispersive x-ray fluorescence (XRF) spectrometer. This bench-top XRF has an autosampler and the ability to flush the analysis chamber with helium, thus allowing routine analysis from Na to U. In addition, subcontracts with two outside collaborators have boosted the core's capabilities in two new areas to include extended X-ray absorption spectroscopy (XAS) of aquifer particles for Fe and As and detailed characterization of bacterial species interacting with As using routine and novel microbial techniques.

On behalf of the projects working in Bangladesh (projects 2, 3, 4, 5, 7) 7500 samples and solutions were analyzed by HR-ICP-MS. In support of project 5 work in New Hampshire and Maine, 1240 analyses by HR-ICP-MS and 60 analyses by XRF were made for As, Mn, U and additional constituents of potential geochemical interest or health concern. Another 240 analyses by HR-ICP-MS and over 300 sediment samples were analyzed by XRF in support of the field study on increasing the efficiency of the pump and treat operations at Vineland Superfund Site (Proj. 6). For the RTC collaboration with Rockland County Department of Health, 110 analyses for pCO₂ and TCO₂ were made on groundwater samples.

For microbial analyses, we have completed development of a method to extract and purify microbial DNA from aquifer systems for radiocarbon analysis. We can now collect, extract, and purify over 100 µg of carbon from groundwater. The DNA has now been shown to be free of impurities. We have collected samples from 4 sites in Bangladesh. Initial results show that recent recharge is not the source of organic carbon driving microbial respiration in high arsenic aquifers. This work will be submitted for publication in 2011. Concurrently, we have also developed and lab-tested a method to collect phospholipid fatty acids (PLFAs) from groundwater. This method will be field tested in 2011 and provide another test for constraining carbon cycling in the subsurface. In addition, we are going to use the purified DNA for metagenomic analyses.

This past year, the core laboratory also generated synchrotron-based X-ray absorption spectroscopy data for preserved aquifer material. These analyses have included time series of 40 microprobe µSXRF scans for Fe, As, S, Mn, Ca, K and 15 samples analyzed for Fe and As speciation by XANES/EXAFS during micro-column experiments conducted at the synchrotron to test potential mechanisms for mobilization of As from aquifer solids From Bangladesh.

Manuscripts involving collaborators supported by Core C:

Argos, M., T Kalra, PJ Rathouz, Y Chen, B Pierce, F Parvez, T Islam, A Ahmed, M Rakibuz-Zaman, R Hasan, G Sarwar, V Slavkovich, A van Geen, J Graziano, H Ahsan, A prospective

- cohort study of arsenic exposure from drinking water and all-cause and chronic disease mortality in Bangladesh, *The Lancet*, DOI:10.1016/S0140-6736(10)60481-3, 2010.
- Wovkulich, K., Mailloux, B. J., Lacko, A., Keimowitz, A. R., Stute, M., Simpson, H. J., Chillrud, S.N., 2010. Chemical Treatments for Mobilizing Arsenic from Contaminated Aquifer Solids to Accelerate Remediation. *Applied Geochemistry*, 25: 1500–1509. PMID: PMC2976553. doi:10.1016/j.apgeochem.2010.08.001
- Garnier, J.-M., F. Travassac, V. Lenoble, J. Rose, Y. Zheng, M. Hossain, S. Chowdhury, A. Biswas, K.M. Ahmed; Z. Cheng, A. van Geen, Temporal variations in arsenic uptake by rice plants: The role of iron plaque in paddy fields of Bangladesh irrigated with groundwater, *Science of the Total Environment*, 408, 4185-4193, 2010.
- Leber J, MM Rahman, KM Ahmed, B Mailloux, A van Geen, Contrasting influence of geology on *E. coli* and arsenic in aquifers of Bangladesh, *Ground Water* doi: 10.1111/j.1745-6584.2010.00689.x, 2010.
- Mladenov N, Zheng Y, Miller MP, Nemergut DR, Legg T, Simone B, Hageman C, Rahman MM, Ahmed KM, McKnightt DM, Dissolved organic matter sources and consequences for iron and arsenic mobilization in Bangladesh aquifers, *Environmental Science and Technology*, 44, 123-128, 2010.
- Aziz, Z, M. Stute, R. Versteeg, P. Schlosser, MR Huq, KM Ahmed, A van Geen, Distribution of As in shallow Bangladesh aquifers of Bangladesh controlled by desorption and flushing: An evaluation at the village-scale using a 3-D groundwater flow model, submitted to *Water Resources Research*, November 2010.
- Aziz, Z., B. Bostick, Y. Zheng, M.R Huq, M.M. Rahman, K.M. Ahmed, and A. van Geen, Suppression of arsenic release to shallow groundwater of Bangladesh by reduced sulfur, resubmitted to *Environmental Science and Technology*, October 2010.
- Benbear L, A Tarozzi, A Pfaff, HB Soumya, KM Ahmed, A van Geen, Bright lines, risk beliefs, and risk avoidance: Evidence from a randomized intervention in Bangladesh, submitted to *American Economic Journal: Applied Economics*, October 2010.
- van Geen A, KM Ahmed, Y Akita, MJ Alam, PJ Culligan, J Feighery, A Ferguson, M Emch, V Escamilla, P Knappett, AC Layton, BJ Mailloux, LD McKay, JL Mey, ML Serre, PK Streatfield, J Wu, M Yunus, Fecal contamination of shallow tubewells in Bangladesh inversely related to arsenic, resubmitted to *Environmental Science and Technology*, September 2010.
- Chen Y, JH Graziano, F Parvez, M Liu, V Slavkovich, T Kalra, M Argos, T Islam, A Ahmed, M Rakibuz-Zaman, R Hasan, D Levy, A van Geen, and H Ahsan, Arsenic exposure from drinking water and cardiovascular disease mortality: A prospective cohort study in Bangladesh, submitted to *British Medical Journal*, October 2010.
- Wagner PJ, R Foster, JF Stolz, MB Scholz, K Wovkulich, GA Freyer, A van Geen, SN Chillrud, Y Zheng, KM Ahmed, BJ Mailloux, Worldwide diversity and occurrence of arsenite transporter *acr3(2)* suggests an important and overlooked pathway for arsenate reduction, submitted to *Environment Microbiology Reports*, May 2010.

Students supported in part by the Biogeochemistry Core over the past year

Kathleen Radloff, Earth & Environmental Engineering, Columbia, PhD June 2010.
Zahid Aziz, Earth & Environmental Sciences, Columbia, PhD December 2010.
Khalid Khan, Mailman School of Public Health, Columbia, PhD September 2010.
Ivan Mihajlov, Earth & Environmental Sciences, Columbia, PhD candidate.
Christine George, Mailman School of Public Health, Columbia, PhD candidate, Audra
Dochenez - Columbia undergraduate student; Radost Stanimirova-Barnard College
undergraduate student; Kimberly Wu- Barnard College undergraduate student; Aanam Aslam-
Barnard College undergraduate student.

Core D: Hydrogeology Core

PIs: Martin Stute, Peter Schlosser, Juerg Matter, Steve Chillrud

The Hydrogeology Support Core provides information on the groundwater and surface water flow and transport regime at our field sites in the US and Bangladesh, and supports projects number 5, 6, 7, and the RTC.

Notable advances for the last period

Field efforts: In January 2010 we conducted a field trip to Bangladesh and continued work on characterizing the deeper, low arsenic aquifers. We sampled wells supplying low arsenic water to the communities in our research area for chemical composition and environmental isotopes such as noble gases and radiocarbon. We found that groundwater in these formations are hundreds to thousands of years old (P7). We also tested the capability of deeper aquifer sediments to absorb arsenic in the case that shallow, high arsenic groundwater would make it into deeper formations by over pumping or well leakage. We developed and set up a system in the field that keeps sediment columns anoxic and flushed them for several weeks with high arsenic water pumped right at the site. The same system was used to determine the quantity of mobilizable arsenic in the shallow aquifer at our intensive field study site K (P5).

Laboratory efforts: We adapted a method on our Ion chromatograph that reduced the measurement time for bromide, a tracer used in many of our field and lab experiments, by a factor of three (P5,6,7).

Sample Measurements: We performed 21 ^3H and 36 ^3He and 24 ^{14}C analyses on samples from wells in Bangladesh (P5,7) and about 100 Br measurements for column experiments (P5,7).

Modeling: The Core supported groundwater flow modeling activities (MODFLOW, MT3D) at site 'X' in Bangladesh (P5&7) in order to quantify the groundwater/surface water interactions. We used tracer data to calibrate the dispersivity used in the model. We were able to reproduce the observed distribution of arsenic at site X with remarkable success (Zahid et al., 2010).

Instrument development: We further studied and finalized the design of a multichannel reagent supply system that has been successfully used by us and subsequently by a consulting firm collaborating with us at the Vineland superfund site (Wovkulich et al., 2010; P6).

All publications listed in Projects 5, 6, 7 and RTC have been supported by the Hydrogeology Core. Of particular relevance are the following:

Aziz, Z., M. Stute, R. Versteeg, P. Schlosser, M.R. Huq, K.M. Ahmed, and A. van Geen. Distribution of As in shallow aquifers of Bangladesh controlled by desorption and flushing: An evaluation at the village-scale using a 3-D groundwater flow model. *Water Resources Research*, submitted, Nov. 2010.

Wovkulich, K., M. Stute, T. Protus, B. Mailloux, S. Chillrud. Injection System for Multi-Well Injection Using a Single Pump, *Ground Water Monitoring and Remediation*, in press, Dec 2010.

Research Translation Core: *Collaborating with Government & the Public: Arsenic & Manganese Exposure via Groundwater*

Co-PI's: Steve Chillrud, Meredith L. Golden

Co-investigators: Joseph Graziano, Martin Stute, Stuart Braman

Over the past year the Columbia SRP RTC has undertaken several activities related to groundwater issues in general and arsenic contamination in particular. We highlight here some of our government and community engagement initiatives.

Columbia RTC continues to partner with government agencies at the county, state, and federal levels in NJ, NY, NH, and ME. At the Vineland Superfund Site, RTC and Project 6 scientists have worked closely with the Remedial Program Manager to determine the most cost effective and expedient way to remove arsenic contamination from the area's groundwater. We have provided feedback to key parts of the external review of this EPA Superfund site based on our work exploring new arsenic remediation techniques. We are currently planning additional field and laboratory work in conjunction with EPA and USACE. In NY, Columbia RTC has continued its collaboration with the Rockland County Department of Health, and the United Water company on a survey of arsenic in the local groundwater in private and public wells. Findings from this study were presented at a community water forum. In addition, over 3000 people attended the annual open house on Columbia's Lamont Campus where we organized hands-on activities highlighting issues of water use and arsenic contamination in the US and Bangladesh. Project scientists working in Maine have also engaged educators, parents, and the local media to promote community involvement in arsenic issues and launched the Strategic Plan for Arsenic Research in Kids (SPARK) program in 5 Maine school districts.

In addition to facilitating project-specific research translation, our RTC continues to play a leadership role in advancing the interactions among SRP-funded universities, federal agencies, and communities concerned with Superfund sites. We are working with researchers at EPA and CDC/ATSDR to determine the most effective way to integrate existing data related to vulnerable populations near Superfund sites. This coordination across agencies is unique and will help create a comprehensive and effective online mapping tool for agencies and other stakeholders concerned with the impact of Superfund sites on nearby communities. It will also assist researchers interested in examining environmental justice issues more closely.

Our RTC scientists are also participating at the national level with initiatives via NARPM and PEPH to coordinate interagency activities focused on Superfund sites. Four project scientists have been nominated to the EPA IRIS review of inorganic arsenic. An RTC geospatial specialist presented a poster at the CDC/ATSDR GIS Day on Innovative Methodologies and Mapping to Assess Vulnerable Populations Near SF sites: GIS Fostering Collaborations. In addition, we have been actively involved with the RTC/CEC Annual Meeting sessions and are committed to help the SRP develop partnerships with EPA and ATSDR as well as implement open access and data sharing policies. Ongoing communications are facilitated by monthly

seminars, the project website, and participation in agency webinars and forums. Finally, one of our SRP project PIs has taken a leave of absence to take a position with UNICEF in Bangladesh to plan and implement the provision of low arsenic drinking water to the entire country.

Students and Postdocs involved in RTC activities in 2010:

Qiang, Yan, PhD student, Queens College

Karen Wovkulich, PhD student, Columbia University

Beth O'Shea, post-doctoral research scientist, Columbia University

Governmental agency contacts:

Vineland Superfund Site: Ron Naman, Nica Klaber, John Frisko, Jon Josephs from EPA Region 2; Steve Creighton and Laura Bittner from USACE- Philadelphia Office; Craig Wallace and Chad Vansciver from NJDEP.

NYS Landfills: Steve Parisio, NYSDEC.

Rockland County Drinking Water Issues: Dan Miller, RCDOH.

Vulnerable Populations Supplemental: Andrew Dent, ATSDR, GRASP; Olivia Harris, ATSDR, Office of Science; Scott Parris, EPA Office of Environmental Justice

General Superfund issues: Nigel Fields, EPA Office of Science Policy; Ronald Landy, EPA Region 3

Maine research on exposures to arsenic in groundwater:

Charles Culbertson, Charles Schalk, Martha Nielsen from USGS Maine Water Science Center; Carole Johnson from USGS Office of Groundwater; Robert Marvinney, Robert Johnston, Marc Loiselle, Daniel Locke from Maine Geological Survey; Andrew Smith, Diane Silverman, Deborah Rice, and Eric Frohberg from Maine Department of Health and Human Services Office of Environmental and Occupational Health Programs; Marcel Belaval from EPA Region I, Drinking Water Program

RTC Core-Supported Publications:

Wovkulich, K., M. Stute, T.J. Protus Sr., B.J. Mailloux, S.N. Chillrud. Injection System for Multi-Well Injection Using a Single Pump. *Ground Water Monitoring and Remediation, In Press, Dec 2010.*

Balletta, M. 2009. Arsenic in Iron Floc and Groundwater Downgradient of Unlined Landfills in Southeastern New York State. B.S. Thesis Facolta' di Scienze Ambientali, Seconda Università degli Studi di Napoli, Caserta, Italy

RTC Core-Supported Presentations:

Braman S. 2010. Rockland County Water Use and Conservation Potential. Presentation at LDEO Public Lecture: Rockland County Water Resources. Columbia University Lamont

Campus, Palisades, NY.

Chillrud, S. 2010. Preliminary Results from Arsenic Groundwater Survey. Presentation at LDEO Public Lecture: Rockland County Water Resources. Columbia University Lamont Campus, Palisades, NY

Chillrud S. and M. Stute. 2010. Vineland Superfund Site: Collaborations between Columbia SRP and EPA Region 2 RPM. Presentation at EPA National Association of Remedial Program Managers meeting. Crystal City, VA.

Graziano, J, 2010: National Academy of Sciences Conference: Effect of Pre-Natal and Neonatal Exposures on Health Outcomes Later in Life. "Consequences of Pre- and Post-Natal Arsenic Exposure in Bangladesh, 10/14/10.

Hei, T. EPA/ NIEHS Workshop on Mineral Fiber: A Science Based Examination of the Mode of Action. Session chair and presenter. December 16th-17th, 2009, Research Triangle Park, NC.

Golden, M. 2010. Working Together: Getting the Best Results Through Partnerships. Panelist. EPA National Association of Remedial Program Managers meeting. Crystal City, VA.

Mailloux, B. and M. Polizzotto. 2010. The Future of Arsenic: Emerging Threats and Scalable Solutions. Convener and presenters. AGU Fall Meeting. San Francisco, CA.

Stute, M. 2010. The "age" of groundwater in Rockland County. . Presentation at LDEO Public Lecture: Rockland County Water Resources. Columbia University Lamont Campus, Palisades, NY.

Stute, M. and B. Mailloux. 2010. Using Water Resource Issues to Engage and Educate. Convener and presenters. AGU Fall Meeting. San Francisco, CA.

RTC Core-Supported Posters:

Chai-Onn, T. 2010. Innovative Methodologies and Mapping to Assess Vulnerable Populations Near SF sites: GIS Fostering Collaborations. Poster presentation at CDC/ATSDR GIS Day, Atlanta, GA.

Golden, M. 2010. Assessment of Populations in Proximity to Superfund Sites: Proposed Partnerships. Poster presented at Partnerships in Environmental Public Health (PEPH) meeting. Research Triangle Park, NC.

Golden, M. 2010. Assessment of Populations in Proximity to Superfund Sites: Proposed Partnerships. Poster presented at EPA National Association of Remedial Program Managers meeting. Crystal City, VA.

Golden, M. and S. Chillrud. 2010. Columbia University SRP Research Translation Core: Highlights of Agency Partnerships and Community Engagement Activities. Poster presented at 2010 Superfund Research Program Annual Meeting. Portland, OR.

Website urls:

Columbia SRP Program website: <http://superfund.ciesin.columbia.edu>

Columbia SRP Water Resources in Rockland County: Planning in a Changing World:

<http://superfund.ciesin.columbia.edu/Rocklandwater/>

Training Core:

PI: Pam Factor-Litvak, PhD

The research projects in the Columbia University SRP have served as a rich training ground for students and post-doctoral fellows. In the past year, the roster of trainees has grown to its largest size ever. We have provided research training to 11 undergraduates, 8 doctoral students, 6 post-doctoral fellows, and have graduated an additional 6 students with doctoral degrees in either Environmental Health Sciences (2) or Earth Science (4). Collectively, the trainees have made enormous contributions to the overall success of our program. The PI of the Training Core has provided guidance to many of our trainees and has been deeply involved in strategizing the research designs of many of the doctoral student dissertation projects.

All of our students actively participate in our monthly seminar series, as well as our off campus retreats with our External Advisory Board. Modest funding from this also core supported a special course in GIS, taught by Mark Becker (from Lamont-Doherty Earth Observatory) at the Mailman School of Public Health. Besides the monthly Superfund Seminar Series, the Training Core also participated in the Annual Granville H. Sewell Distinguished Lecture in Environmental Health Sciences which this year featured Dr. Howard Frumkin, now the Dean of the School of Public Health at the University of Washington, who spent a day with our trainees prior to giving his keynote seminar on the topic of Climate and Health.

In addition, the Training Core continued to offer trainees participation in a web-based course on "Hazardous Waste and Public Health" during the summer semester which can be done by anyone with a computer and internet access from any location and which has proven highly successful in past years. The course includes practical case studies in managing hazardous waste issues as problem-solving exercises for the participants.

Patent Updates: None.

Superfund Site Updates: None.

Contact Information Updates: Updated in the attached file.

Student Information Updates: Embedded within text and also updated in attached excel file