Progress Report: Columbia University SBRP, December, 2006

Highlight #1: Folic acid supplementation lowers blood arsenic by increasing As methylation (Manuscript in preparation)

PI: Mary V. Gamble

Chronic arsenic (As) exposure currently affects more than 100 million people worldwide. Methylation of ingested inorganic arsenic (InAs) to methylarsonic- (MMA) and dimethylarsinic acids (DMA) relies on folate-dependent one carbon metabolism. In a recent, randomized, controlled trial, we analyzed total As and As metabolites in urine and showed that folic acid supplementation resulted in an increase in the proportion of total urinary As excreted as DMA (%uDMA) and a reduction in %uMMA and %uInAs[1,2]. Since DMA has a shorter circulating half-life than other arsenic metabolites, we hypothesized that facilitation of As methylation via folic acid supplementation might lower total blood As (tbAs) concentrations. Methodological advances, using inductively coupled mass spectrometry with a dynamic reaction cell (ICP-MS-DRC) have permitted us to test this hypothesis by measuring total As and As metabolites in blood in 130 participants with low plasma folate (< 9 nmol/L) before and after 12 weeks of supplementation with folic acid (400 µg/d) or placebo. These methodological advances have also led to the discovery that blood As is a biomarker of As exposure that is directly associated with the risk for arsenic-induced skin lesions[3]. Thus, lowering blood As with folic acid could have therapeutic potential to reduce the risk for arsenic-induced illnesses.

Folic acid supplementation reduced MMA in blood (bMMA) by 22.2 ± 2.9 percent (mean ± SE) as compared to placebo (1.24 ± 3.0 percent, $p < 0.0001$). On average, bMMA was reduced from 4.1 ± 2.6 µg/L pre-intervention to 3.0 ± 1.8 µg/L post intervention (mean ± SD) ($p < 0.0001$) for the folic acid group. For the placebo group, corresponding values were 4.0 ± 2.5 vs. 3.8 ± 2.3 µg/L ($p = 0.21$). Eighty-five percent of all participants in the folic acid group experienced a decline in bMMA; 55% of participants in the placebo group experienced a decline in bMMA. Greater declines were observed for individuals who had higher bMMA at baseline than for those that had lower bMMA at baseline. There was no change in DMA in blood; the latter is rapidly excreted in urine as was evidenced by an increase in urinary DMA ($p = 0.01$). InAs in blood decreased by 18.5% for the folic acid group vs. 10.6% for the placebo group ($p = 0.07$). Folic acid supplementation reduced tbAs by 14% vs. 2.5% for the placebo group ($p = 0.02$). Pre- vs. post-intervention tbAs concentrations declined from an average of 9.9 ± 5.1 to 8.2 ± 4.2 µg/L ($P < 0.0001$) for the folic acid group, whereas the placebo group had a modest, nonsignificant decline from 9.6 ± 5.0 to 9.1 ± 4.9 µg/L ($P = 0.2$). The data were similar with further adjustment for age, BMI, and gender.

Population studies indicate that individuals with relatively greater portions of MMA and smaller proportions of DMA in urine are at greater risk for skin lesions, skin and bladder cancer, and peripheral vascular disease[4-8]. Furthermore, studies employing cell culture and animal models suggest that MMA^{III} may be the most cytotoxic and genotoxic As intermediate[9]. The current study indicates that folic acid supplementation lowers total blood As primarily by lowering concentrations of MMA in blood. These findings imply that folic acid supplementation may reduce body stores of As. In conclusion, therapeutic strategies to facilitate As methylation, particularly in populations with a high prevalence of folate deficiency and/or hyperhomocysteinemia such as Bangladesh[10], may lower blood As concentrations, and thereby contribute to the prevention of arsenic-induced illnesses.

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11. Gamble MV, Liu X. Letter re: Urinary creatinine concentrations in the U.S. population: implications for urinary biologic monitoring measurements. Environ Health Perspect 2005;113.

Highlight #2: Arsenic Exposure from Drinking Water and Risk of Premalignant Skin Lesions in Bangladesh: Baseline Results from the Health Effects of Arsenic Longitudinal Study (HEALS) [Ahsan et al. Am J Epidemiol. 2006 Jun 15;163(12):1138-48]

PI: Habibul Ahsan

Millions of people in the world, including more than three million in the United States and more than 50 million in Bangladesh, are chronically exposed to arsenic (As) – a potent human carcinogen. However, our knowledge about the health effects of As exposure at doses <100 µg/L is primarily based on extrapolations from high-dose studies. Most of the studies conducted to date, including cohort studies, have employed retrospective ecological exposure measurements in their dose-response analyses, making individual-level exposure assessment extremely difficult. Using data from nearly 12,000 men and women in Araihazar, Bangladesh, we investigated the effects of As exposure on As-induced skin lesions, a hallmark of As poisoning, for doses ranging from very high to very low measured at the individual level. We also evaluated the influence of key host factors on this association, including body mass index (BMI), gender, and age. Measures of As exposure include urinary creatinine-adjusted As concentration and a time-weighted well water As concentration (TWA) incorporating the information on well use history. Adjusted prevalence odds ratios (PORs), excess relative risk (ERR), and relative excess risk for interaction (RERI) were estimated to assess the main effects of As and its interaction with key host characteristics (BMI, male gender, and age).

Compared to persons drinking water containing <8.1 µg/L of As, adjusted PORs of skin lesions for those drinking water with 8.1-40.0, 40.1-91.0, 91.1-175.0, and 175.1-864.0 µg/L of As were 1.91 (95% CI: 1.26-2.89), 3.03 (95% CI: 2.05-4.50), 3.71 (95% CI: 2.53-5.44), and 5.39 (95% CI: 3.69-7.86), respectively. While creatinine-adjusted urinary As does not directly correspond to TWA categories, the elevated risk was statistically significant also for the second lowest category. In linear dose-response analyses, we estimated that a 10 µg/L increase in tube well water As concentration was associated with an ERR of 0.122 (95% CI: 0.087-0.171), i.e., those exposed to As doses of 10 µg/L had a 1.22 times higher risk of developing skin lesions compared to those with zero dose.

Males appeared to be disproportionately more susceptible to skin lesions than females at higher levels of TWA. The RERI estimates for the interaction of male gender and top four TWA quintiles were 2.7 (95% CI: -0.0, 5.4), 5.9 (95% CI: 0.8-10.9), 8.9 (95% CI: 1.7-16.1), and 11.6 (95% CI: 2.2-21.0). The corresponding attributable proportion due to interaction (AP = RERI/POR for joint exposures) is 39%, 52%, 64%, and 61%, which corresponds to the fraction of skin lesion risk among males with each higher level of As exposure that can be attributable to the synergistic effect of male gender and As. At each level of TWA, older participants were more susceptible to skin lesions than their younger counterparts. At each level of TWA, we also observed a trend for the adjusted PORs for skin lesions to be higher for participants with lower levels of BMI.

This study reports a strong dose-response effect of As exposure on skin lesion risk in Bangladesh. This dose-response effect was uniformly evident in several statistical models appropriate for analyzing cross-sectional data. We found that well water As concentrations <50 µg/L (the currently permissible limit in Bangladesh and

other countries and in the US until very recently) is associated with an increased risk for skin lesions. Previous studies in other countries, including those in Bangladesh and West Bengal, had failed to show any increased risk at the lower As dose range, partly because those studies lacked sufficient sample size at the low-level As exposure. We found that male, older, and/or thinner participants were more likely to be affected by As exposure. These findings need to be taken into consideration for risk assessment and policy-making decisions.

Highlight #3: Folate deficiency, hyperhomocysteinemia and hypomethylation of genomic DNA are risk factors for arsenic-induced skin lesions: A nested case-control study in Bangladesh (Manuscript in preparation)

PI: Mary V. Gamble

Chronic arsenic (As) exposure currently affects more than 100 million people worldwide. In Bangladesh alone, this exposure is affecting approximately 50 million residents. Individuals exposed to As are at increased risk for cancers of the skin, bladder, lung, and liver. Non-cancer health outcomes include stroke, ischemic heart disease, and neurologic consequences. The current study focuses on premalignant As-induced skin lesions.

Methylation of ingested inorganic arsenic (InAs) to methylarsonic- (MMA) and dimethylarsinic acids (DMA) relies on folate-dependent one carbon metabolism. DMA has a shorter circulating half-life than other As metabolites, and is readily excreted in urine. Therefore, methylation of As facilitates excretion of As in urine. There is considerable interindividual variability in As methylation, and mounting evidence indicates that nutritional status influences this variability. For example, we have previously found that there is a very high prevalence of hyperhomocysteinemia in Bangladesh[1] and that folate deficiency and hyperhomocysteinemia are associated with a reduced capacity to methylate arsenic[2]. In a recent, randomized, controlled trial, we discovered that folic acid supplementation resulted in an increase in the proportion of total urinary As excreted as DMA (%uDMA) and a reduction in %uMMA and %uInAs[3]. To begin to assess the potential impact on health outcomes, we here test the hypothesis that low plasma folate and/or hyperhomocysteinemia are risk factors for subsequent development of arsenic-induced skin lesions (SLs). Because folate and homocysteine influence DNA methylation, and previous studies employing cell culture and animal models indicate that arsenic (As) exposure also influences DNA methylation, we also investigated whether genomic hypomethylation of peripheral blood leukocyte DNA (PBL DNA) is a risk factor for SLs.

We conducted a nested case-control study in Araihazar, Bangladesh. The study participants were a subset of the 11,746 men and women of the HEALS cohort study[4] between the ages of 18 and 65 years who were recruited between October 2000 and May 2002, and who continue to be followed at two year intervals. A total of 316 incident SL cases (i.e. people who were free of SLs at baseline, but developed SLs by 2 years after recruitment) and 316 controls were individually matched for gender and age (within 5 years), and frequency matched for water As (within 100 µg/L). Folate, homocysteine and DNA methylation were assessed in samples that had been collected at the baseline visit, at which time all participants were free of SLs. Genomic methylation of PBL DNA was determined using a [3H]-methyl incorporation assay.

Conditional logistic regression analyses found the odds ratios (95% C.I.s) for subsequent development of SLs for participants who, at baseline, had either marginal folate status (plasma folate < 9 nmol/L), high Hcys (> 10.4 µmol/L), or hypomethylated PBL DNA (below the median) were 1.8 (1.21 – 2.81; p = 0.005), 1.68 (1.2 - 2.5; p = 0.01), and 1.8 (1.17 – 2.80; p = 0.008), respectively. The significance of these results were not altered after further adjustment for covariates.

Folate deficiency, hyperhomocysteinemia, and hypomethylation of genomic PBL-DNA appear to be independent risk factors for arsenic-induced skin lesions. Given that there is a very high prevalence of hyperhomocysteinemia in Bangladesh, particularly among males, a careful assessment of the risks and benefits of a country-wide folic acid intervention is warranted.

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2. Gamble MV, Liu X, Ahsan H et al. Folate, homocysteine and arsenic metabolism in Bangladesh. Environ Health Perspect 2005;113:1683-8.

3. Gamble M, Liu X, Ahsan H et al. Folate and Arsenic Metabolism: A double-blind placebo controlled folic acid supplementation trial in Bangladesh. Am J Clin Nutr 2006;84:1093-101.

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Highlight #4: The Role of Arsenic in Melanoma Treatment

P.I. Tom Hei

The incidence of melanoma has substantially increased worldwide over the last 40 years. Although melanoma accounts for only 10% of the skin cancers, it is responsible for at least 80% of the mortality cases. Approximately 8,000 Americans died of melanoma in 2005 and 62,200 new cases of melanoma have been diagnosed in 2006. Advanced melanomas are highly refractory to conventional radio- and chemotherapy and no effective therapy exists to inhibit metastatic spread of this cancer.

Arsenite is a two-sided sword: on the one hand, it is a well established human carcinogen and, on the other hand, it has been used successfully in the treatment of acute promyelocytic leukemia by inducing apoptosis. We have previously shown that only ~20% of human melanoma cell lines are conducive to apoptosis by arsenite treatment alone (Vladimir and Hei, 2004 & 2005). A recent clinical trail in the use of single regimen of arsenite trioxide in the treatment of metastatic melanoma fails to produce any significant improvement in clinical outcome. These findings suggest that multi-modality regimen is required in the design of treatment strategy.

The tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) has been shown to have great anti-tumor potential via induction of apoptosis in a wide variety of human TRAIL-Receptor-1 (TRAIL-R1/DR4) and Receptor-2 (TRAIL-R2/DR5) -positive cancer cells including melanomas. In contrast, most normal human cells often contain high levels of decoy receptors TRAIL-R3 and TRAIL-R4 on cell surface, thus, preventing induction of apoptotic signaling. Many metastatic tumors, including melanomas, acquired the secondary resistance to TRAIL-mediated apoptotic signaling (almost 60% of tumor cell lines are resistant to recombinant TRAIL). Besides increasing the number of decoy receptors, such resistance may occur at different points of the TRAIL-induced death signaling pathway. Suppression of surface expression of the death receptors (TRAIL-R1/DR4 and TRAIL-R2/DR5), dysfunction of death receptors due to mutations, suppression of the pro-apoptosis caspase-8 or caspase-3 functions, over-expression of inhibitors of apoptosis, such as cFLIP (cellular FLICE inhibitory protein), XIAP (X-linked inhibitor of apoptosis), Bcl-2 and Bcl-xL directly correlates with resistance to TRAIL in many types of cancer. Especially, progression in melanoma is often linked with decreased surface expression of TRAIL-R1/R2. On the other hand, general activation of the NF-κB, PI3K-AKT and BRAF-MEK-ERK signaling pathways, which are characteristic features of advanced tumors, including metastatic melanomas is connected with protection against TRAIL-mediated apoptosis via up-regulation of gene expression of anti-apoptotic proteins.

Our previous studies have demonstrated that sodium arsenate may dramatically affect signaling pathways in melanoma cells and differentially regulate AP-1/cJun, NF-κB and STAT3 transcription factor activities that control expression of numerous genes for proliferation, survival and apoptosis. Sodium arsenite is known to suppress both the IKK-NF-κB and JAK2-STAT3 signaling pathways and to activate the MAPK/JNK-c-Jun pathways, thereby committing some cancers to undergo apoptosis. In our recent studies, we found sodium arsenite treatment up-regulated TRAIL-mediated apoptosis in human and mouse melanomas by increasing surface levels of death receptors, TRAIL-R1 and TRAIL-R2, through increased translocation of these proteins from cytoplasm to the cell surface. In addition, activation of c-Jun and suppression of NF-κB by sodium arsenite resulted in upregulation of the endogenous *TRAIL*- and downregulation of the *cFLIP* gene expression (which encodes one of the main anti-apoptotic proteins in melanomas). This results in cFLIP protein degradation and acceleration of TRAIL-induced apoptosis. Similar effects can also be achieved using RNAi to suppress *cFLIP* expression. In contrast, suppression of cyclooxygenase-2 (COX-2) by RNAi or NS398 substantially increased levels of both TRAIL-induced and arsenite-induced apoptosis. Finally, over-activation of the protein kinase AKT increased melanoma survival in cell culture and dramatically accelerated growth of melanoma transplant *in vivo*, highlighting a role of AKT suppression for effective anti-cancer treatment.

A better understanding in the apoptotic signaling pathways induced by arsenic treatment in melanoma cells with concurrent modulator of pro-apoptotic and suppression of anti-apoptotic pathways will provide a useful mechanistic rationale for effective treatment design for this often fatal cancer.

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Ivanov, V.N., , and Hei, T.K., Dual treatment with COX-2 inhibitor and sodium arsenite leads to induction of surface Fas Ligand expression and Fas-Ligand-mediated apoptosis in human melanoma cells. *Exp. Cell Research* 312: 1401-1417, 2006.

Ivanov, V.N., Ze'ev, R., and Hei, T.K., Opposite roles of FAP-1 and dynamin in the regulation of Fas (CD95) translocation to the cell surface and susceptibility to Fas ligand-mediated apoptosis. *J. Biol. Chem*. 281: 1840-1852, 2006.

Ivanov, V. N. and Hei, T.K., Sodium arsenite accelerates TRAIL-mediated apoptosis in melanoma cells through upregulation of TRAIL-R1/R2 surface levels and down-regulation of cFLIP expression. *Exp. Cell Research* 312: (In press 2006).

Project 1: Genotoxic Mechanisms of Arsenic in Mammalian Cells
P.I.: Tom K. Hei

The overall goals of this project focus on 1) the mechanisms of the DNA damaging effects of arsenic in mammalian cells, particularly the role of mitochondrial DNA mutations and the subsequent induction of reactive oxygen and reactive nitrogen species; and 2) the mechanism for arsenic-induced apoptosis (programmed cell death) in melanoma cells.

During the current funding period, and as part of our continuous genotoxicity studies of arsenic using the human-hamster hybrid (A_L) cells, we sequenced the entire 16,284 base pair mitochondrial DNA of the Chinese hamster (*Cricetulus griseus*). The sequence was obtained by generating six overlapping PCR products encompassing the entire mtDNA genome. The 13 protein coding sequence of hamster mitochondrial genome, the rRNA genes, and the 22 tRNAs, are all encoded in the same order and on the same strand as other species examined. The genome is, by nuclear DNA standard, remarkably compact, with no introns and very few non-coding regions.

Using the human hamster hybrid (A_L) cells, we examined the effects of arsenic treatment on mitochondria metabolic function and, in particular, whether arsenic exposure altered mtDNA. Arsenic treatment (0.25 μg/ml for 15, 30 and 60 days) decreased cytochrome c oxidase function and increased citrate synthase activity. These phenotypic alterations were partially reversed by the addition of the free radical scavenger, dimethyl sulfoxide (DMSO). Furthermore, arsenic depleted the mtDNA copy number and there was an increased incidence of large heteroplasmic mtDNA deletions after arsenic exposure. It should be noted that mtDNA isolated periodically from the same continuously treated cultures did not consistently display the same deletion, indicating that the mitochondrial genome was subjected to repeated and continuous damage when exposed to arsenic. These data support the theory that the mitochondria, and particularly mtDNA, are important mediators of the mutagenic effects of arsenic in mammalian cells.

Arsenite is a two-sided sword: on the one hand, it is a well established human carcinogen and, on the other hand, it has been used successfully in the clinic in the management of acute promyelocytic leukemia by inducing apoptosis. Sodium arsenite is known to suppress both the IKK-NF-κβ and JAK2-STAT3 signaling pathways and to activate the MAPK/JNK-c-Jun pathways, thereby committing some cancers, including melanomas, to undergo apoptosis. Since malignant melanoma is highly refractory to conventional radio- and chemotherapy, we examined the efficacy of combined signal modulating drugs in the presence of arsenite to increase susceptibility of cancer cells to apoptotic signaling. There is evidence that arsenite treatment upregulated surface levels of death receptors, TRAIL-R1 and TRAIL-R2, through increased translocation of these proteins from cytoplasm to the cell surface. In addition, activation of c-Jun and suppression of NF-κβ by sodium arsenite resulted in up-regulation of the endogenous *TRAIL*- and downregulation of the *cFLIP* gene expression (which encodes one of the main anti-apoptotic proteins in melanomas). This results in cFLIP protein degradation and acceleration of TRAIL-induced apoptosis. Similar effects can also be achieved by using RNAi, to suppress cFLIP expression.

Arsenic is an important environmental carcinogen that affects millions of people worldwide through contaminated water supplies. For decades, arsenic was considered a non-genotoxic carcinogen. Using the highly sensitive A_L mutation assay, we showed previously that arsenic is indeed a potent gene and chromosomal mutagen and mitochondria are a primary target in arsenic-induced genotoxic response. 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. On the other hand, melanoma is often a deadly disease due to the lack of effective treatment options. Despite the dramatic increase in the incidence of malignant melanoma in the past decades, the molecular mechanisms of its progression and extreme resistance to treatment, which kill cells by induction of programmed cell death (apoptosis), remain largely unknown. Our present study, however, indicates that arsenic can also be a two sided sword and could, potentially, benefit thousands of melanoma patients each year who fail conventional therapeutic regimens.

Publications:

Ivanov, V.N., , and Hei, T.K., Dual treatment with COX-2 inhibitor and sodium arsenite leads to induction of surface Fas Ligand expression and Fas-Ligand-mediated apoptosis in human melanoma cells. *Exp. Cell Research* 312: 1401-1417, 2006.

Ivanov, V.N., Ze'ev, R., and Hei, T.K., Opposite roles of FAP-1 and dynamin in the regulation of Fas (CD95) translocation to the cell surface and susceptibility to Fas ligand-mediated apoptosis. *J. Biol. Chem*. 281: 1840-1852, 2006.

Patridge, M., Davidson, M.M., and Hei, T.K., The complete nucleotide sequence of Chinese hamster (Cricetulus griseus) mitochondrial DNA sequence. DNA Sequence (In Press 2006)

Ivanov, V. N. and Hei, T.K., Sodium arsenite accelerates TRAIL-mediated apoptosis in melanoma cells through upregulation of TRAIL-R1/R2 surface levels and down-regulation of cFLIP expression. *Exp. Cell Research* 312: (In press 2006).

Project 2: A Cohort Study of Health Effects of Arsenic Exposure in Bangladesh
P.I.: Habibul Ahsan

This prospective cohort study recruited 11,746 adults (with 98% response rate) in Araihazar, Bangladesh, during 2000-2002 to investigate the health effects of arsenic exposure, with an initial focus on skin lesions and skin cancers, and also to establish a biorepository for future studies. All 5,966 contiguous tube wells were tested for arsenic within a well-defined area of approximately 26 square kilometers and, all 65,876 people in the study area using these wells were enumerated. Findings from this pre-cohort study survey have been published [van Geen et al., 2002 and 2003; Parvez et al., 2005]. All biological samples and baseline questionnaire data have been processed and stored for all 11,746 cohort members. A description of the study design and cohort was published [Ahsan et al., 2005]. Analysis of total urinary arsenic for all baseline samples and also arsenic metabolites in a subset of 1,200 individuals (skin lesion cases and controls) has been completed. Using baseline cross-sectional data on arsenic exposure and prevalent skin lesion cases, we conducted a full dose-response analysis of the relationship between arsenic exposure and risk of skin lesions and factors modifying this dose-response effect. These novel results, with major public health significance, are being published [Ahsan et al., 2006; Argos et al., in press 2007; Chen et al., 2006]. Full dietary data from all cohort members was also collected using a validated meal-based dietary questionnaire [Chen et al., 2004].

Between October 2002 and May 2004, we completed our first 2-yearly follow-up visit of the cohort. We collected follow-up data on nearly 100% (11,743 of 11,746) of the baseline cohort. A total of 11,326 individuals completed the follow-up interview and clinical evaluations; 313 were not available and 104 died. Approximately 98% of participants with a completed follow-up interview (11,107 of 11,326) provided a urine sample. The follow-up data on all 11,743 individuals have been computerized. All 11,107 follow-up urine samples have been analyzed for urinary total arsenic. In addition, we also analyzed blood arsenic levels for the newly identified skin lesion cases from this follow-up visit and their matched controls. Findings from this prospective investigation of the association between blood arsenic and skin lesion risk are being published [Chen et al., submitted].

Between October 2004 and November 2006, we completed our second 2-yearly follow-up visits. Among the 11,642 living baseline cohort participants, 11,640 were contacted for a second follow-up visit. We completed a follow-up interview on 10,930; 215 participants unavailable at the first follow-up were still unavailable, 380 participants were newly unavailable, and 115 had died. Approximately 98% of participants who completed a follow-up interview (10,713 of 10,930) provided a urine sample. All second follow-up questionnaire data has been computerized and urine samples processed. The third 2-year follow-up of the cohort is underway.

In addition to the above-mentioned components, the findings and resources from this prospective cohort study have 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.

SBRP-related 2006 publications:

Ahsan, H., Y. Chen, et al. (2006). "Arsenic exposure from drinking water and risk of premalignant skin lesions in Bangladesh: baseline results from the Health Effects of Arsenic Longitudinal Study." Am J Epidemiol 163(12): 1138-48.

Argos, M., M. G. Kibriya, et al. (2006). "Gene expression profiles in peripheral lymphocytes by arsenic exposure and skin lesion status in a Bangladeshi population." Cancer Epidemiol Biomarkers Prev 15(7): 1367-75.

Chen, Y., P. Factor-Litvak, et al. (2006). "Nutritional influence on risk of high blood pressure in Bangladesh: a population-based cross-sectional study." Am J Clin Nutr 84(5): 1224-32.

Chen, Y., J. H. Graziano, et al. (2006). "Modification of risk of arsenic-induced skin lesions by sunlight exposure, smoking, and occupational exposures in Bangladesh." Epidemiology 17(4): 459-67.

Chen Y, Hakim ME, Parvez F, Islam T, Rahman AM, and Ahsan H. Arsenic exposure from drinking water and carotid artery intima-media thickness in healthy young adults in Bangladesh. J Health Pop Res 2006; 24(2): 000-000.

Hafeman, D., H. Ahsan, et al. (2006). "Betel quid: Its tremor-producing effects in residents of Araihazar, Bangladesh." Mov Disord 21(4): 567-71.

Hall, M., Y. Chen, et al. (2006). "Blood arsenic as a biomarker of arsenic exposure: results from a prospective study." Toxicology 225(2-3): 225-33.

Parvez, F., Y. Chen, et al. (2006). "Prevalence of arsenic exposure from drinking water and awareness of its health risks in a Bangladeshi population: results from a large population based study." Environ Health Perspect 114(3): 355-9.

In Press:

Argos M, Parvez F, et al. (In press). "Influence of socioeconomic factors on the effects of arsenic on premalignant skin lesions – results from the Health Effects of Arsenic Longitudinal Study (HEALS)." American Journal of Public Health.

Chen Y, Factor-Litvak P, et al. (In press). "Association between Arsenic Exposure from Drinking Water and Blood Pressure in Bangladesh: a population-based cross-sectional study." American Journal of Epidemiology.

Ahsan H, Chen Y, et al. (In press). "Arsenic metabolism, genetic susceptibility and risk of pre-malignant skin lesions." Cancer Epidemiology Biomarkers Prevention.

Kibriya MG, Argos M, et al. (In press). "Gene expression patterns in peripheral mononuclear cells due to selenium supplementation among patients with arsenical skin lesions in Bangladesh population." Toxicology Letters.

Chen Y, Graziano JH, et al. (In press). "A Prospective Study of Blood Selenium Levels and The Risk of Arsenic-related Skin Lesions." Cancer Epidemiology Biomarkers Prevention.

Heck J, Graziano JH, et al. (In press). "Consumption of Folate-Related Micronutrients and Metabolism of Arsenic among Bangladeshis Chronically Exposed to Arsenic." American Journal of Clinical Nutrition.

Mahata J, Argos M, et al. (In press). "Effect of Selenium and Vitamin E Supplementation on Plasma Protein Carbonyl Levels in Patients with Arsenic Related Skin Lesions." Nutrition and Cancer.

Li Y, Chen Y, et al. (In press). "Serum levels of the extracellular domain of the epidermal growth factor receptor in individuals exposed to arsenic in drinking water in Bangladesh." Biomarkers.

Submitted for Publication:

Chen Y, van Geen A, et al. (Submitted for publication). "Reduction in Urinary Arsenic Levels in Response to Arsenic Mitigation Efforts in Araihazar, Bangladesh."

Hafeman D, van Geen L, et al. (Submitted for publication). "Association between manganese exposure through drinking water and infant mortality in Bangladesh."

Heck J, Graziano JH, et al. (Submitted for publication). "Factors Associated with Anemia in an Arsenic-Exposed Population in Bangladesh."

Parvez F, Brnadt-Rauf PW, et al. (Submitted for publication). "Non-malignant Respiratory Effects of Chronic Arsenic Exposure from Dinking Water in Bangladesh: A Molecular Epidemiological Study."

Students supported at least in part by Project 2:

Supervision

Post-Doctoral (Columbia University)

2003-2005 **M. G. Kibriya, MD, PhD,** Postdoctoral Research Scientist, Mailman School of Public Health, Columbia University. *Current position:* Research Associate (Assistant Professor), Department of Health Studies, the University of Chicago.

Pre-Doctoral (Columbia University)

Primary Advisor / Sponsor

2002-2005 **Yu Chen**, Thesis: Arsenic exposure, dietary factors and hypertension among Bangladesh population. *Current position:* Assistant Professor, Department of Environmental Medicine, New York University School of Medicine.

2003-2006	**Julia Heck**, Thesis: Protein intake, arsenic exposure and risk of arsenical skin lesions. *Current position:* Research Fellow, International Agency for Research on Cancer (IARC), Lyon, France.
2004-	**Danella Hafeman**, Thesis: Under development.
2004-	**Maria Argos**, Thesis: Under development.

Project 3: Consequences of Arsenic and Manganese Exposure on Childhood Intelligence (New Title)

PI: Joseph Graziano

This project builds upon our discovery that arsenic and manganese exposure from drinking water have adverse effects on intelligence in children. Our past work has occurred in Bangladesh, where water used for drinking and cooking contains naturally elevated concentrations of both arsenic and manganese. This past year we published findings of two cross-sectional studies of Bangladeshi children.

The first study examined the relationship between water manganese and child intelligence in 142 children who lived where water arsenic was extremely low, but water manganese was elevated (Wasserman et al, 2006a). Children in the highest quartile for water manganese, whose drinking water contained more than 1 mg/L (i.e., more than twice the WHO guideline level of 0.4 mg/L) performed significantly worse on an adaptation of the WISC-III, an intelligence test, than children in the lowest quartile (water manganese < 0.2 mg/L).

Our second publication (Wasserman et al, 2006b) expands on our previous work in Bangladesh, which found that water arsenic adversely affected intelligence in 10 year-old children. In this study, a random sample of 301 six year old children who were drinking water with wide ranges of arsenic and manganese concentrations were evaluated. After adjustment for covariates including sociodemographic factors, blood lead, and water manganese concentrations, water arsenic levels were adversely associated with child intelligence.

In parts of the U.S., e.g., New Hampshire, where household wells are the source of water, arsenic concentrations often exceed the EPA guideline levels. Our findings in Bangladesh led us to ask whether similar effects of arsenic might be observed in the U.S.. We have therefore now launched a new study of 500 fourth grade children in NH to determine whether exposure to arsenic impairs intellectual functioning. New staff have been recruited at the University of New Hampshire, our collaborating institution, and trained by Columbia faculty. Four school boards have expressed support, and work is now ongoing in eight elementary schools in New Hampshire.

Simultaneously, our work with children in Bangladesh continues. We have expanded our research to determine whether exposure to arsenic and manganese has an adverse effect on motor function. In addition, by providing deep, low arsenic and low manganese wells after assessments of motor and cognitive functioning, we will determine whether the adverse effects of arsenic and manganese are reversible.

Finally, we completed a study concerning the transfer of arsenic and its metabolites to the fetus during pregnancy. In Matlab, Bangladesh, 104 pregnant women were recruited, and biological samples were collected at delivery. We discovered that

the total blood arsenic concentration in the newborn is higher than that in maternal blood at the time of birth. Analyses of blood arsenic metabolites – a new method developed by our Trace Metals Core Lab – revealed that cord blood metabolite levels mimicked those seen in maternal blood. Of particular importance, blood contained much higher concentrations of inorganic arsenic and monomethyl arsenic (MMA), than urine, indicating that maternal and fetal tissues are exposed to much more of these toxic arsenic species than previously imagined (Hall et al, submitted).

Students whose research is supported at least in part by Project 3:

At the Mailman School of Public Health:

Marni Hall, Ph.D. student in Environmental Health Sciences
Khalid Khan, Dr.PH student in Environmental Health Sciences

At the University of New Hampshire:

Patricia Jarema, Ph.D. student in Research Administration and Management

Publications:

Wasserman, GA, Liu, X, Parvez, F, Ahsan, H, Levy, D, Factor-Litvak, P, Kline, J, van Geen, A, Slavkovich, V, LoIacono, NJ, Cheng, Z, Zheng, Y, Graziano, JH: Water manganese exposure and children's intellectual function in Araihazar, Bangladesh. Environ Health Perspect 114: 124-129, 2006a.

Wasserman, G, Liu, X, Parvez, F, Ahsan, H, Factor-Litvak, P, Kline, J, van Geen, A, Slavkovich, V, LoIacono, N, Levy, D, Cheng, Z, Graziano, JH: Water arsenic exposure and intellectual function in six year-old children in Araihazar, Bangladesh. Environ Health Perspect, in press, 2006b, available on-line.

Hall, M, Gamble, MV, Liu, X, Slavkovich, S, Levy, D, Cheng, Z, van Geen, A, Yunus, M, Rahman, M, Pilsner, JR, Graziano, J: Determinants of arsenic metabolism: Blood arsenic metabolites, plasma folate, B_{12} and homocysteine concentrations in maternal-newborn pairs. Submitted, 2006.

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

PI: Mary V. Gamble

There is considerable variability in progression from arsenic (As) exposure to clinical manifestations of disease, and nutritional status may account for some of this variability. Methylation of ingested inorganic arsenic (InAs) to methylarsonic- (MMA) and dimethylarsinic acids (DMA) relies on folate-dependent one carbon metabolism and facilitates urinary As elimination. As a new component of this SBRP, Project 4 expands upon our R01 supported studies (Nutritional Influences on Arsenic Toxicity or NIAT) *which demonstrated that folic acid supplementation increases As methylation and lowers total blood As concentrations*.

The first aim of this proposal utilizes the repository of biological samples established by the Cohort Study (Project #2) to conduct a nested case-control study. We here test the hypothesis that at the time of enrollment, participants who subsequently went on to develop As-induced skin lesions (SLs) had lower indices of one-carbon metabolism (e.g. low plasma folate and/or high homocysteine) as compared to non-skin lesion controls. This study includes 316 incident SL cases (i.e. cases were free of SLs at baseline, but developed SLs by 2 years after recruitment), and 316 control subjects individually matched to cases for gender, age (within 5 years) and frequency matched for water arsenic (within 100 µg/L). As preliminary data for our R01 renewal, we also analyzed genomic methylation of peripheral blood leukocyte DNA (PBL DNA) using a [3H]-methyl incorporation assay.

Conditional logistic regression analyses revealed that the odds ratios (95% C.I.s) for subsequent development of SLs for participants who, at baseline, had marginal folate status (plasma folate < 9 nmol/L), high Hcys (> 10.4 µmol/L), or hypomethylated PBL-DNA (below the median) were 1.8 (1.21 – 2.81; p = 0.005), 1.68 (1.2 - 2.5; p = 0.01), and 1.8 (1.17 – 2.80; p = 0.008), respectively. These studies indicate that folate deficiency, hyperhomocysteinemia, and hypomethylation of genomic PBL-DNA are risk factors for arsenic-induced skin lesions.

For our second specific aim, we wished to address a fundamental question: To what extent do urinary As metabolites reflect As metabolites in the circulation? We planned to measure total As and As metabolites in blood and in urine from 375 newly enrolled study participants. Banked blood samples from a 12 week randomized, controlled folic acid supplementation trial (part of the NIAT study) were available for immediate analysis by the Trace Metals Core Laboratory. These analyses reveal that the average percentage of total As in urine vs. blood, respectively, for each metabolite are 15.3 ± 7.1 vs. 25.6 ± 3.4 %InAs, 12.8 ± 4.6 vs. 40.0 ± 5.3 %MMA, and 72 ± 8.5 vs. 34.4 ± 6.1 %DMA. Consistent with our understanding that methylation to DMA facilitates urinary As elimination, the relative distributions of As metabolites in urine do not closely reflect their distributions in blood. *These analyses further led to the discovery that folic acid supplementation lowers total blood As concentrations by reducing MMA in blood and increasing DMA in urine* (see Highlight #1). Therapeutic strategies to facilitate As methylation may lower blood As concentrations, and thereby contribute to the prevention of arsenic-induced illnesses.

List of Publications Directly Relevant to this Project

<u>Manuscripts published or in press</u>:

Gamble MV, Ahsan H, Slavkovich V, Liu X, Parvez F, Hussain I, Momotaj H, and Graziano JH. Folate and cobalamin deficiencies and hyperhomocysteinemia in Bangladesh. Am J Clin Nutr 2005; 81(6):1372-1377.

Gamble MV and Liu X. Letter of Correspondence re: Barr et al., Urinary creatinine concentrations in the u.s. Population: implications for urinary biologic monitoring measurements. Env Health Perspect 2005; 113:A442.

Gamble MV, Liu X, Ahsan H, Pilsner JR, Ilievski V, Slavkovic V, Parvez F, Levy D, Factor-Litvak P, Graziano J. Folate, homocysteine and arsenic metabolism in Bangladesh. Env Health Perspect 2005; 113(12):1683-1688.

Gamble, MV, Liu X, Ahsan H, Pilsner JR, Ilievski V, Slavkovich V, Parvez F, Chen Y, Levy D, Factor-Litvak P, Graziano JH. Folate and Arsenic Metabolism: A double-blind placebo controlled folic acid supplementation trial in Bangladesh, Am J Clin Nutr 2006; 84:1093-1101.

Submitted and in review:

Pilsner JR, Liu X, Ahsan H, Ilievski V, Slavkovich V, Levy D, Factor-Litvak P, Graziano JH, Gamble MV. Genomic DNA methylation: Influences of folate, arsenic and selenium in Bangladeshi adults (EHP).

Ahsan H, Chen Y, Kibriya MG, Slavkovich V, Parvez F, Jasmine F, Gamble MV, Graziano JG. Arsenic metabolism, genetic susceptibility and risk of pre-malignant skin lesions in Bangladesh (Ca Epi Biomark & Prev).

Hall M, Gamble MV, Liu X, Slavkovich V, Levy D, Cheng Z, van Geen A, Yunus M, Rahman M, Pilsner JR, Graziano JH. Determinants of arsenic metabolism: Blood arsenic metabolites, plasma folate, B12 and homocysteine concentrations in maternal-newborn pairs (EHP).

Heck JE, Gamble MV, Chen Y, Graziano JH, Slavkovich V, Parvez F, Baron JA, Howe G, and Ahsan H. Consumption of folate-related micronutrients and metabolism of arsenic in Bangladesh (Am J Clin Nutr, accepted pending revisions).

Selected Recent Abstracts:

Pilsner JR, Liu X, Ahsan H, Ilievski V, Slavkovich V, Levy D, Factor-Litvak P, Graziano JH, Gamble MV. Genomic DNA Methylation: Influences of Folate and Arsenic in Bangladeshi Adults. Presented at the International Society of Environmental Epidemiology and Exposure meeting in Paris, September 2006. This poster (from hundreds of posters and presentations) was awarded first prize.

Gamble MV, Pilsner JR, Liu X, Ahsan H, Ilievski V, Slavkovich V, Parvez F, Factor-Litvak P, and Graziano JH. Methylation of arsenic and DNA: A double-blind, placebo controlled trial of folic acid supplementation in Bangladesh. FASEB Summer Research Conference, Folic Acid, B12 & One Carbon Metabolism, Indian Wells, CA, August 2006.

Project 5: Arsenic mobilization in Bangladesh Groundwater
Since the renewal on April 1, 2006, new title:
Project 5: Mobilization of Natural Arsenic in Groundwater

Y. Zheng, M. Stute, and A. van Geen

Th past year resulted in the publication of three papers. Jung and Zheng (2006) developed and calibrated a method to speciate As sorbed on solid phases by experimenting with ferrihyrite and goethite. While on sabbatical leave, Zheng guest-edited a mini-monograph entitled "*Occurrence and Health Effect of Arsenic in China*" consisting of six papers to appear in Environmental Health Perspective in early 2007. Dr. Zheng co-authored one of these reports concerning arsenicosis occurrence rates in endemic regions of China where > 400,000 well As were surveyed (Yu et al., in press). Zheng (2007) reviews geochemical evidence for crustal heterogeneity of As and suggests that its linkage to worldwide groundwater As occurrence warrants further investigation. Four additional manuscripts (2 submitted, 3 in prep) are based on advances made in 2006:

Mineralogy and Mobility of Fe and As in Meghna River Sediments in Bangladesh

Post-doc Saugata Datta (now assistant professor at W. Georgia State Univ.) undertook a geochemical study of sediment samples taken along the Meghna River in January 2003 (DATTA et al., submitted). Arsenic discharged from groundwater is

trapped and recycled in the delta, and represents a source of As to groundwater on the time scale of thousands of years.

Graduate student Hun Bok Jung (Jung et al., in prep) is conducting a follow-up study of the mechanism causing enrichment of As along the Meghna River. Groundwater Fe, As, and PO_4 showed systematic attenuation from well water to riverbank porewater, indicating trapping of As in a reactive barrier formed by Fe precipitation.

Microbes and arsenic mobilization in deep Pleistocene aquifer of Bangladesh: limited roles of iron reduction

Graduate student Ratan K. Dhar examined the role of microbial arsenate and iron reduction in the mobilization of As (DHAR et al., in prep.) by incubating Pleistocene sediment inoculated with wild-type *Shewanella* sp. ANA-3 and a mutant *Shewanella* sp. ANA-3 (ARM1) Significantly, *Shewanella* converted the tightly bound As in the solid phase to a mobilizable form. Microbial processes responsible for this conversion may be critical to the vulnerability of Pleistocene aquifers of Bangladesh.

Hydrological Control of As Concentrations in Bangladesh Groundwater

The heterogeneous distribution of dissolved arsenic in Bangladesh complicates understanding of its release from the sediment matrix into the groundwater, as well as the design of mitigation strategies. Based on the relationship between dissolved As concentrations and ($^3H/^3He$) ages we propose that spatial variability of As concentrations in shallow (<20 m deep) aquifers can to a large extent be attributed to heterogeneity in the local groundwater flow. (Stute et al., 2006)

Occurrence of As, Mn and Rn in 787 private wells in Greater Augusta, Maine

Graduate students Hun Bok Jung and Qiang Yang analyzed 787 samples for their chemical compositions collected from private wells in Greater Augusta, Maine as a baseline for a detailed hydrogeochemical study (JUNG et al., in prep.). Groundwater As concentrations ranged from <0.01 μg/L to 325 μg/L, with 245 samples (31%) > 10 μg/L. Elevated As wells are mostly located in Silurian meta-sedimentary rock.

Students and Post-docs whose research is supported at least in part by Project 5:

Allan Horneman, Earth Environmental Engineering, Columbia, PhD, 2005
Ratan Dhar, Earth and Environmental Sciences, CUNY, PhD, 2006
Saugata Datta, Post-doc fellow, Columbia University, Earth Institute
Hun Bok Jung, 3rd yr PhD candidate, Earth and Environmental Sciences, City University of New York (CUNY)
Karrie Radloff, 2nd PhD candidate, Environmental Engineering, Columbia
Qiang Yang, 1st yr candidate, Earth and Environmental Sciences, CUNY

Publications:

Datta S., Mailloux B., Hoque M. A., Jung H.-B., Stute M., Ahmed K. M., and Zheng Y. (submitted) Enrichment of Arsenic in Sediments from the Meghna River Bank in Bangladesh: Implication for Recycling of Arsenic. *Proc Natl Acad Sci U S A*.

Dhar R. K., Zheng Y., Saltikov C. W., Radloff K. A., Mailloux B., and van Geen A. (in prep.) Microbes and arsenic mobilization in deep Pleistocene aquifer of Bangladesh: limited roles of iron reduction.

Jung H. B., Yang Q., Culbertson C. W., Marvinnney R. G., Loiselle M. C., Locke D., Cheek H., Thibodeau H., Hess C. T., and Zheng Y. (in prep.) Geochemical Characteristics of Groundwater from Domestic Wells in Greater Augusta, Maine, USA. *Environmental Science & Technology*.

Jung H. B. and Zheng Y. (2006) Enhanced recovery of arsenite sorbed onto synthetic oxides by l-ascorbic acid addition to phosphate solution: calibrating a sequential leaching method for the speciation analysis of arsenic in natural samples. *Water Research* **40**(11), 2168.

Stute, M., Zheng, Y., Schlosser, P, Horneman, A. Dhar, R.K., Datta, S., Hoque, M. A., Seddique, A. A. , Shamsudduha, M., Ahmed, K. M., andvan Geen, A. (2006) Hydrological Control of As Concentrations in Bangladesh Groundwater. Water Res. Res, submitted.

Yu G.-Q., Sun D.-J., and Zheng Y. (2006) Health Effect of Exposure to Natural Arsenic from Groundwater and Coal in China: An Overview of Occurrence. *Environ Health Perspect* **in press**.

Zheng Y. (2007) The heterogeneity of arsenic in the crust: A linkage to occurrence in Groundwater. *Quaternary Sciences (Chinese)* **27**(1).

Project 6: *Mobilization of anthropogenic arsenic in groundwater*
P.I.s: Steven Chillrud, Martin Stute, H. James Simpson, Brian Mailloux, John Stolz

Project 6 focuses on investigations of arsenic behavior at the Vineland Superfund site, a former arsenic biocide manufacturing plant in Vineland, NJ. During this past year we focused on laboratory characterization of sandy aquifer solids in preparation for future laboratory and field studies that will be targeted on increasing the efficiency of pump and treat remediation of contaminated aquifers. Our results show that aquifer samples with 220 ppm As can have > 95% of the arsenic mobilized by a 1 molar sodium phosphate solution, suggesting that the As contamination is surface bound in a form that could be readily mobilized. Arsenate was the primary form of solid phase As based on a few aquifer solid samples analyzed by x-ray absorption spectroscopy (XAS). An offsite aquifer sample had only ~1 ppm As suggesting that background levels of arsenic in this geographic area are quite low. Samples from well below the water table obtained from cores of aquifer solids at two locations indicated total As concentrations ranged from 20 to 60 ppm in contaminated zones to well below 6 ppm in areas that appear uncontaminated.

Additional laboratory experiments explored the effectiveness of several amendments to mobilize particle-bound As: 1) Acetate additions were made to laboratory incubations of synthetic groundwater and aquifer solids to stimulate natural microbe communities. Microbes were expected to use the electron donors, thereby creating more reducing conditions and cause increases in the mobility of arsenic. 2) Base titrations were carried out with the expectation that increases in pH would lead to increases in arsenic mobility due to changes in the electrostatic attraction between arsenate species and their binding sites. 3) Experiments with varying concentrations of sodium phosphate were carried out since phosphate is a good analog compound for arsenate and competes for similar surface sites. 4) Experiments with varying concentrations of oxalic acid, a naturally occurring acid component of soils, were carried

out since it is known to dissolve iron oxyhydroxides, which can serve as significant reservoirs for sorbed arsenic.

Some conclusions from these characterization experiments include: A) Arsenic concentrations in the contaminated aquifer solids can be greatly elevated above background levels (by one to two orders of magnitude). B) In areas affected by the contaminant plume, a large fraction of sediment arsenic is easily extractable. This indicates that making amendments to the subsurface could be effective in enhancing the release of arsenic from aquifer solids. C) Microbial activity can enhance release of arsenic from the solids but appears to be less effective than adding chemical amendments. D) Raising the pH of the system had only minor impact on the mobility of arsenic and does not appear as effective as other treatment options explored here. E) Both phosphate and oxalic acid were promising as chemical amendments for further exploration and possible in situ use. Lower concentrations of oxalic acid than phosphate were needed to mobilize at least 80% of the sediment arsenic. We plan to further test these ideas in column experiments and pilot field studies during the coming year.

Students and Postdocs involved in studies in 2006:
Alison Keimowitz, PhD 2005, Earth and Environmental Science, currently Postdoc at Columbia University
Karen Wovkulich, 2nd year graduate student, Earth and Environmental Science, Columbia University
Tara Fiechter-Russo, senior undergraduate student, Barnard College
Shane Riordan, summer intern, High School teacher

2006 Publications and meetings:

Keimowitz, A.R., B. J. Mailloux, P. Cole, M. Stute, H. J. Simpson, S.N. Chillrud. Laboratory investigations of sulfate reduction as a groundwater arsenic remediation strategy. Submitted to Environ. Sci. Tech.

Wovkulich, K. A. R. Keimowitz, M. Stute, H.J. Simpson, Y. Zheng, Z. Cheng, S. Chillrud. 2006. Arsenic Cycling and Transport Issues at Vineland Chemical Superfund Site. Poster, *Geological Society of America Meeting*, Philadelphia, Pa, October 2006.

Keimowitz, A.R., M. Stute, H.J. Simpson, S. Chillrud. 2006. Effect of hydrogeological heterogeneity on spatial distribution and release of arsenic beneath a landfill. Poster at *Geological Society of America*, Fall meeting, Philadelphia, PA, October 2006.

Project 7: Mitigation of Arsenic Mobilization in Groundwater (new title)
P.I.: Alexander van Geen

Co-Investigators: Yan Zheng, Martin Stute, Zhongqi Cheng, Peter Schlosser, Andrew Gelman, and Alex Pfaff

This year's contributions of 13 published papers/manuscripts in press and 11 submissions under review can be divided under 3 headings (1) exploration of the mechanisms of As mobilization, (2) As mitigation and policy, and (3) collaborations with public health scientists. The following paragraphs highlight studies under (1) and (2) where Project 7 played a leading role.

Considerable attention was devoted to documenting the high-degree of spatial variability of As concentrations in Bangladesh groundwater using a simple device, coined the needle-sampler, that simultaneously collects groundwater and aquifer

particles. The approach is a descriptive but necessary first step towards elucidating the processes that control As mobilization. Field studies using the needle-sampler resulted in a paper by van Geen et al. (2006) that appeared in *Chemical Geology* and another paper by Metral et al. submitted to *Geochemical Transactions* demonstrating an association of elevated As concentrations with relatively impermeable surface layers that inhibit dilution by local recharge. The importance of this relationship was revealed earlier by the study of Aziz et al. that relied on a simple geophysical technique to map the distribution of impermeable surface layers within the Araihazar study area. The needle-sampler was also used to collect groundwater and aquifer particles to directly measure the rate of As release under close-to-natural conditions during a series of year-long incubations. This work submitted by Radloff et al. to *Environmental Science and Technology* confirms the importance of local hydrology with respect to groundwater As levels in the sense that measured rates of As release were not higher in depth intervals where the highest As concentrations were measured.

The fate of As supplied to rice paddies by shallow irrigation wells was also studied under Project 7 and resulted in a paper by van Geen et al. (2006) and another submitted manuscript by Travassac et al. The two studies show that As is significantly enriched in soil and soil-water of rice paddies that are irrigated with high-As groundwater with, thankfully, very limited transfer of this input to the rice grain.

Contributions from Project 7 under the heading of arsenic mitigation in Bangladesh were of two types this year. First, the encouraging response of the study population of Araihazar to well-labeling and the installation of community wells was documented in the survey conducted by Opar et al. (2007). The development of simple technology using SMS messaging via mobile-phones to guide the installation of new wells by targeting safe aquifers using an extensive existing database was demonstrated in a pilot described by van Geen et al. in a paper accepted by the *J. of Health, Population, and Nutrition*. A paper by van Geen et al. submitted to *J. Environmental Science and Health* demonstrates with detailed time-series, however, that deep community wells can fail and therefore must be periodically monitored. Also significant is the expected publication as a Policy Forum in the December 15, 2006 issue of *Science* of a consensus report co-signed by 10 scientists, 3 of whom are from Columbia, pointing out the importance of low-technology solutions for As mitigation in Bangladesh, in particular, continued well-testing.

Submitted Manuscripts:

Métral, J., L. Charlet, S. Bureau, S. B. Mallik, S. Chakraborty, K.M. Ahmed, M.W. Rahman, Z. Cheng, and A.van Geen, Impact of local recharge on arsenic concentrations in shallow aquifers of Chakdaha, India, and Araihazar, Bangladesh, submitted to *Geochemical Transactions*, December 2006.

Radloff, K.A., Z. Cheng, M.W. Rahman, K.M. Ahmed, B.J. Mailloux, A.R. Juhl, P. Schlosser, and A. van Geen. Mobilization of arsenic during one-year incubations of grey aquifer sands from Araihazar, Bangladesh, submitted to *Environmental Science and Technology*, December 2006.

Chen, Y., A. van Geen , J. Graziano , A. Pfaff, M. Madajewicz, F. Parvez , I. Hussain, Z. Cheng, V. Slavkovich, T. Islam, and H. Ahsan, Reduction in urinary arsenic levels in response to arsenic mitigation in Araihazar, Bangladesh, submitted to *Environmental Health Perspectives*, October 2006.

van Geen, A., Z. Cheng, Q. Jia, A. A. Seddique, M. W. Rahman, M. M. Rahman, and K. M. Ahmed, Monitoring 51 deep community wells in Araihazar, Bangladesh, for up to 5

years: Implications for arsenic mitigation, submitted to *Journal of Environmental Science and Health*, October 2006.

Travassac, F.,J.-M. Garnier, J. Rose, M.S. Hossain, S. H. Chowdhury, K.M. Ahmed, Y. Zheng, Z.Cheng, and A. van Geen, Accumulation of arsenic in soil water, iron plaque, and roots in rice paddies over a growing season in Araihazar, Bangladesh, submitted to *Science of the Total Environment*, September 2006.

Cheng, Z., B.M. Buckley, B. Katz, W. Wright, R. Bailey, K.T. Smith, A. van Geen, Arsenic in tree rings at a highly contaminated site, revision sent to *Science of the Total Environment*, September 2006.

Dhar, R.K., Y. Zheng, M. Stute, A. van Geen, Z. Cheng, M. Shanewaz, M. Shamsudduha, M.A. Hoque, M.W. Rahman, and K.M. Ahmed, Temporal variability of groundwater chemistry in shallow and deep aquifers of Araihazar, Bangladesh, submitted to *Geochim. Cosmochim. Acta*, June 2006.

Weinman, B., Goodbred, S.L., Zheng, Y., Aziz, Z., Singhvi, A.K., Nagar, Y.C., Steckler, M., A. van Geen, Arsenic concentrations in shallow groundwater of Araihazar, Bangladesh: Part I. Geological control through floodplain evolution, submitted to *Water Resources Research*, January 2006.

Aziz, Z., A. van Geen, R. Versteeg, A. Horneman, Y. Zheng, S. Goodbred, M. Steckler, M. Stute, B. Weinman, I. Gavrieli, M.A. Hoque, M. Shamsudduha, and K.M. Ahmed, Arsenic concentrations in shallow groundwater of Araihazar, Bangladesh: Part II Hydrologic control reflected in the electromagnetic conductivity of soils, submitted to *Water Resources Research*, January 2006.

Stute, M., Y. Zheng, P. Schlosser, A. Horneman, R.K. Dhar, M. A. Hoque, A. A. Seddique, M. Shamsudduha, K. M. Ahmed, and A. van Geen, Hydrological control of As concentrations in Bangladesh groundwater, revision sent to *Water Resources Research*, February 2006.

Madajewicz, M., A. Pfaff, A. van Geen, J. Graziano, I. Hussein, H. Momotaj, R. Sylvi, and H. Ahsan, Can information alone both improve awareness and change behavior? Arsenic contamination of groundwater in Bangladesh, revision submitted to *Journal of Development Economics*, May 2006.

Peer-reviewed publications in 2006:

Opar, A., A. Pfaff, A. A. Seddique, K. M. Ahmed, J. H. Graziano, and A. van Geen, Responses of 6500 households to arsenic mitigation in Araihazar, Bangladesh, *Health & Place* 13, 164-172, 2007.

Chen, Y., M. Hall, J. H. Graziano, V. Slavkovich, A.van Geen, F. Parvez, and H. Ahsan, A prospective study of blood selenium levels and the risk of arsenic-related premalignant skin lesions, *Cancer Epidemiology, Biomarkers and Prevention*, in press November 2006.

Ahmed, M.F., S. Ahuja, M. Alauddin, S. J. Hug, J.R. Lloyd, A. Pfaff, T. Pichler, C. Saltikov, M. Stute, and A. van Geen, Ensuring safe drinking water in Bangladesh, *Science* (Policy Forum), in press December 2006.

van Geen, A., M. Trevisani, J. Immel, Md. Jakariya, N. Osman, Z. Cheng, A. Gelman, and K.M. Ahmed, Targeting low-arsenic groundwater with mobile-phone technology in Araihazar, *J. Health Population and Nutrition*, in press March 2006.

Hall, M., Y. Chen, H. Ahsan, V. Slavkovich, A. van Geen, F. Parvez and J. Graziano, Blood arsenic as a biomarker of arsenic exposure: results from a prospective study, *Toxicology*, available online 18 June 2006.

van Geen, A., Y. Zheng, Z. Cheng, H. Yi, R. Dhar, J. M. Garnier, J. Rose, A. A. Seddique, M. A. Hoque, and K.M. Ahmed, Impact of irrigation with groundwater elevated in arsenic on rice paddies in Bangladesh, *Science of the Total Environment*, 367, 769-777, 2006.

Ahsan, H., A., Y. Chen, F. Parvez, L. Zablotska, M. Argos, A.Z.M. Iftikhar Hussain, H. Momotaj, D. Levy, Z. Cheng, V. Slavkovich, A. van Geen, G.R. Howe, J.H Graziano, Arsenic exposure from drinking water and risk of premalignant skin lesions in Bangladesh: Baseline results from the Health Effects of Arsenic Longitudinal Study (HEALS), *American Journal of Epidemiology*, available on-line on April 19, 2006; doi: doi:10.1093/aje/kwj154.

Chen, Y., J. H. Graziano, F. Parvez, I. Hussain, H. Momotaj, A. van Geen, G. R. Howe, H. Ahsan, Modification of risk of arsenic-induced skin lesions by sunlight exposure, smoking, and occupational exposures in Bangladesh, *Epidemiology* 17, 459-467, 2006.

Parvez F, Chen Y, Argos M, Hussain AZMI, Momotaj H, Dhar R, van Geen A, Graziano JH, Ahsan H, Prevalence of arsenic exposure from drinking water and awareness of its health risks in a Bangladeshi population: Results from a large population-based study, *Environmental Health Perspectives* 114, 355-359, 2006.

Ahsan H, Chen Y, Parvez F, Argos M, Hussain AI, Momotaj H, Levy D, Van Geen A, Geoffrey HA, Graziano J, Health Effects of Arsenic Longitudinal Study (HEALS): Description of a multidisciplinary epidemiologic investigation, *J. Exposure Science and Environmental Epidemiology* 16, 191-205, 2006.

van Geen, A., Y. Zheng, Z. Cheng, Z. Aziz, A. Horneman, R. K. Dhar, B. Mailloux, M. Stute, B. Weinman, S. Goodbred, A. A. Seddique, M. A. Hoque, and K. M. Ahmed, A transect of groundwater and sediment properties in Araihazar, Bangladesh: Further evidence of decoupling between As and Fe mobilization, *Chemical Geology* 228, 85-96, 2006.

Cheng, Z., A. van Geen, A. A. Seddique, and K.M. Ahmed, Response to comments on "Limited temporal variability of arsenic concentration in 20 wells monitored for 3 years in Araihazar, Bangladesh", *Environmental Science and Technology*, 40, 1718-1720, 2006.

Wasserman, G. A., X. Liu, F. Parvez, H. Ahsan, D. Levy, P. Factor-Litvak, J. Kline, A. van Geen, V. Slavkovich, N.. J. LoIacono, Z. Cheng, Y. Zheng, J. H. Graziano, Water manganese exposure and children's intellectual function in Araihazar, Bangladesh, *Environmental Health Perspectives*, 114, 124-129, 2006.

Students supported at least in part under Project 7 over the past year

Allan Horneman, Earth & Environmental Engineering, Columbia, PhD, 2006.
Kathleen Radloff, Earth & Environmental Engineering, Columbia, PhD candidate.
Zahid Aziz, Earth & Environmental Science, Columbia, PhD candidate.
Amy Schoenfeld, Earth & Environ. Sci. and Journalism, Columbia MS 2005.
Jessica Leber, Earth & Environ. Sci. and Journalism, Columbia MS candidate.
M. Shahadat Hossain, School of Continuing Education, Columbia University.
Anya Manning, Environmental Sciences, Barnard College undergraduate.
Thomas Bidal d'Asfelt, High school student, Paris, France.

Administrative Core
Director: Joseph Graziano
Deputy Director: Alexander van Geen

A. General Activities: The Administrative Core continues to function smoothly, and was instrumental in directing the creation and submission of a successful competitive renewal application of our SBRP program. Dr. Graziano, the Program Director, and Dr. van Geen, the Associate Director, communicate virtually every working day with regard to the integration of our biomedical and non-biomedical research programs. 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. Our monthly two-hour seminars (one hour biomedical and one hour non-biomedical) are exceptionally well attended. We believe that our SBRP is unique with regard to the extent that these two dimensions of the program are highly integrated.

In March, 2006 our External Advisory Committee convened for two days at Columbia University's Lamont-Doherty Earth Observatory to review our progress. The composition of the committee has been revised somewhat to reflect the new program aims, and now includes only three members of the former committee: a) Chien-Jen Chen, Committee Chair, and Chairman of the Graduate Institute of Taiwan; b) Andrew Gelman, Professor of Statistics at Columbia University; and c) Alan Welch, Geochemist, U.S. Geological Survey (USGS). New members include: d) Zoltan Szabo, Research Hydrologist, USGS; e) Margaret Karagas, Chair, Section of Biostatistics and Epidemiology, Dartmouth University; f) Allan Smith, Professor of Epidemiology, University of California, Berkeley; g) X. Chris Le, Professor of Public Health Sciences, University of Alberta; h) Peggy O'Day, Associate Professor of Natural Sciences, University of California, Merced; and i) James Davis, USGS. Several of these senior scientists were selected because they are also potential future collaborators. This newly assembled committee was extremely instrumental in guiding the future direction of many of the projects and core laboratories. The committee will reconvene in the Spring of 2007.

Research Translation Core
Collaborating with Government & the Public: As & Mn Exposure via Groundwater
Co P.I.s: H. James Simpson, Meredith L. Golden
Co-investigators: J.H. Graziano, M. Becker, M. Stute, S. Chillrud, Y. Zheng, A. van Geen

The Research Translation Core (RTC) provides a framework for sustained communication among research projects, cores, governmental agencies, and interested parties through monthly seminars, the program website (www.superfund.ciesin.columbia.edu), meetings, and the Lamont Open House. The RTC government partnerships encompass activities in four states (NJ, NY, NH, ME) and include collaborations with county, state, and federal agencies. The central theme is to work directly with selected government agencies responsible for minimizing human exposure to arsenic (As) and manganese (Mn) from groundwater. The RTC facilitates the identification and sharing of geophysical, geochemical, hydrological, and socio-demographic data by public and private parties in order to integrate these into

Geographic Information Systems (GIS) to enhance both monitoring and regulatory decisionmaking.

In collaboration with Steve Parisio (NYSDEC), the RTC is evaluating landfills as potential sources for elevated groundwater As and Mn through joint field and laboratory measurements. The transport of As from landfills is being monitored using the chemical composition of iron (Fe) floc deposits (see Parisio et al., 2006). This innovative approach should be appreciably less costly than using monitoring wells. The RTC has also provided NYSDEC Region 3 with expertise and staff to integrate their data with high-resolution socio-economic data into GIS. RTC investigators participated in national meetings on arsenic issues related to landfills (Tucson, 13-14 February 2006 and Boston, 3-4 October 2006; see http://www-apps.niehs.nih.gov/sbrp/3/arsenic/index.cfm for presentations).

The RTC is assisting Paul Heisig (USGS) with a multi-year assessment of groundwater quality and quantity to evaluate the impacts from high population growth in Rockland County, NY. Our scientists have discussed these issues directly with Dan Miller (RC-DOH) and county legislators. The SBRP Hydrogeology Core Lab tested several groundwater samples for environmental tracer measurements, expertise that otherwise was not readily available. These will be used to help determine the potential for contamination from surface waters by framing the time-scale of groundwater recharge at selected locations in the aquifer. The RTC is also providing USGS with molecular-based bacterial source testing and tracking methods to help determine the cumulative extent of leaking by sewers that may be degrading groundwater quality. Key contacts for Project 6 & 7's work at the Vineland Superfund site include Ron Naman (EPA), Steve Creighton (USACE), Glen Stevens (USACE), and Steve Gillespie (Sevenson Environmental Services) with whom there have been several meetings to share results and discuss the aims and needs of ongoing and future work. Contacts for Project 5's work on groundwater As in New Hampshire and Maine include Chuck Culbertson (USGS), Bob Marvinney (ME Geological Survey), Andy Smith (ME DOH), and Bernie Lucie (NH DES). Printed materials on Arsenic in Drinking Water and Arsenic Health Information have been distributed to the relevant school boards. Finally, key contacts for Project 5 & 7's work in Bangladesh include Sk. Akhtar Ahmad (NIPSOM), Md. Nurul Osman (National Arsenic Mitigation Information Center), Khawaja M. Minnatullah (World Bank), and Rick Johnston (UNICEF). Finally, Columbia is organizing with University of Dhaka and UNDP a symposium on "New Findings Concerning the Health Effects and Geochemistry of Arsenic" for February 2007.

Ahmed, M. F., et al. "Ensuring Safe Drinking Water in Bangladesh". Anticipated publication: 15 December 2006, Science, Vol. 314.

Parisio, S., A.R. Keimowitz, H.J. Simpson, A. Lent, and V. Blackman. Arsenic-rich iron floc deposits in seeps downgradient of solid waste landfills, Soil & Sediment Contamination 15: 443-453, 2006.

Zaks, David. "Text messaging for Safe Water". Published online 27 October 2006. http://www.worldchanging.com/archives/005170.html (reader comments included). Link to the application: http://www.ldeo.columbia.edu/welltracker/

Core A: Data Management Core

The data management core provides support to projects 2 (Arsenic Cohort Study), 3 (the children's studies), and 4 (One-Carbon Metabolism, Oxidative Stress, and Arsenic Toxicity Studies) under this SBRP. In general, the core provides the following services:

1. Consultations on questionnaire design
2. Programming (database systems, desktop and web based data-entry screens programmed with validation and logic checking)
3. Data-entry services
4. Data storage on secure Windows servers
5. Creation of datasets
6. Management of all aspects of systemization of data
7. Query and issue tracking

Over the past five years the data management staff provided selected services from the above list to each of the three projects with which it works. The following chart summarizes the tasks that were performed.

Service	**Description**	**Project**
Questionnaire design	Consulted with project managers	Projects 2 & 3
Created a multi-user Microsoft Access database/data-entry system	• Questionnaire data for 3 phases of Arsenic cohort study data approx 34,500 • Questionnaire data for 3 child studies • laboratory (blood based and urine) results	Project 2 Project 3 Projects 2,3 & 4
Data-entry		Projects 2 & 3
Maintenance of secure database and web servers		Projects 2,3 & 4
Ongoing creation of targeted datasets	Variables requested by PIs and statistician	Projects 2,3 & 4
Managed process/data flow	Used Issue tracking system, Query tracking system and customized programs to detect missing data and logical data inconsistencies.	Projects 2,3 & 4

Recently the data management team moved the database platform from Microsoft Access to Microsoft SQL server. By changing the database system we are ensuring a more stable environment, less prone to the database corruption problems that often occur with Access. In addition, Microsoft SQL server allows for secure web-based access to data. All SBRP data were moved into the new environment.

In preparation for the child studies that will take place in New Hampshire and Bangladesh, new tables were designed and programmed to store the expected data. Furthermore, secure, web-based data-entry screens have been programmed to accept both test and questionnaire data for these studies. The following table summarizes the status of the forms:

Project	Test/Questionnaire	Status
Children's study in Bangladesh	WASI/maternal IQ	Done
	Bruininks/motor function	Done
	WISC/child IQ	In progress
	Home tracking	Done
Children's study in NH	WASI/maternal IQ	Done
	WISC/child IQ	In progress
	Home/covariates	Done
	Well/water consumption	In progress

Looking forward, the data management core is planning to program a web-based data-entry system for cohort follow-up 3 in early 2007. We are thus positioning ourselves to take advantage of expected increased Internet connectivity in Bangladesh.

Core B: Trace Metals Core Laboratory

PI: Joseph Graziano
Laboratory Director: Vesna Slavkovich

The primary purpose of the Trace Metals Core Laboratory is to provide Center investigators with the capability to obtain analyses of biological samples for a broad array of metals including: lead, mercury, arsenic, iron, manganese, cadmium, copper, zinc, chromium, sodium, cobalt, platinum, potassium and others. In addition, the facility provides method development for these analyses, standardization, and quality control.

In addition to conducting routine analyses of thousands of biological samples from projects 2, 3 and 4, this lab has recently adapted and/or developed two new analytical methods that have led to significant research breakthroughs. Until now, the measurement of arsenic in blood samples has been considered to be of little value, since blood arsenic concentrations are exceedingly low and undetectable by conventional graphite furnace atomic absorption methods. Using inductively coupled mass spectrometry, with a dynamic reaction cell (ICP-MS-DRC), the Trace Metals lab has developed a new method for arsenic in blood; using this method, everyone's blood arsenic level is detectable. Working with investigators in Project #2's large cohort study in Bangladesh, we have demonstrated that blood arsenic is an extremely useful biomarker of arsenic exposure, in that it is strongly associated with water arsenic, urine arsenic, and skin lesion status (Hall et al, 2006a). This method has enabled investigators in Project #4 to discover that folic acid supplementation to arsenic-exposed residents of Bangladesh produces a significant decline in blood arsenic concentration, due to facilitation of arsenic methylation and elimination.

This lab has also used a combined high pressure liquid chromatographic (HPLC) method in conjunction with ICP-MS-DRC to analyze the concentrations of individual arsenic metabolites in blood. Until now, no epidemiologic studies have been able to examine arsenic metabolites in blood; they have relied on analyses of urine, in which arsenic concentrations are much higher. We have made two novel observations using this new blood method. First, in Project #3, in a study of mother-cord pairs of blood samples, and maternal urine samples, we discovered that blood contains much higher proportions of inorganic arsenic and monomethylarsenic (MMA), the more toxic species, than urine; this occurs because dimethylarsenic (DMA), the less toxic fully methylated

form, is much more readily excreted by the kidney. Second, in Project #4, we have discovered the decline in blood arsenic that occurs in response to folic acid treatment (mentioned above) is due almost entirely to a decline in the blood concentration of MMA! Collectively, these observations have enormous public health significance, and indicate that folic acid treatment may represent a new therapeutic modality for arsenic-exposed people.

Students involved with this work:

Marni Hall, Ph.D. student in Environnmental Health Sciences, Mailman School
J. Richard Pilsner, Ph.D. student in Environnmental Health Sciences, Mailman School

Publications: Virtually every publication listed for Projects 2, 3 and 4 has relied on the Trace
Metals Core Laboratory.

Core C: Biogeochemistry Core
PI: Alexander van Geen
Co-investigators: Yan Zheng, Steve Chillrud, Brian Mailloux,
Outside collaborators: Benjamin Bostick (Dartmouth U.), John Stolz (Duquesne U.)

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 (biomedical projects 2, 3 and 4 and earth science projects 5, 6 and 7) and trains students and post-docs. Many of the publications and exciting new discoveries under these 6 projects are directly linked to contributions from this core. Sample preparation and 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). In addition, subcontracts with two outside collaborators have boosted the core's capabilities in two new areas to include extended X-ray absorption fine structure spectroscopy (EXAFS) of aquifer particles for Fe and As and detailed characterization of bacterial species interacting with As using 16S rRNA techniques.

On behalf of biomedical projects 2, 3, 4 a total of 1600 new groundwater samples collected from Araihazar, Bangladesh, with support from project 7 have been analyzed by HR ICP-MS for As and Mn. In support of project 5, nearly 800 groundwater samples collected in Maine were analyzed by HR ICP-MS for As, Mn, U and additional constituents of potential geochemical interest or health concern. A total of nearly 700 groundwater and leachate samples for material collected from the Vineland Superfund sites were analyzed by HR ICP-MS on behalf of project 6. Under the monitoring program of community wells in Bangladesh supported under project 7, a total of 300 groundwater samples were analyzed for a broad suite of constituents, including elements of potential concern. Another 300 bi-weekly samples from an array of purposely installed very shallow monitoring wells within Araihazar, Bangladesh, have been analyzed by HR ICP-MS.

On the microbial side, DNA was extracted from contaminated and non-contaminated sediment and clone libraries were constructed using primers b27f and u1492r to amplify 16s rDNA in material collected from the Vineland site (project 6). Distinct differences were observed in the microbial population of the two locations within the landfill. We are now analyzing the diversity across an arsenic gradient with 16s

rDNA and *ArrA* primers. In support of projects 5 and 7, DNA was extracted 10 aqueous water samples from Bangladesh and analyzed by clone libraries, terminal restriction fragment length polymorphism (T-RFLP), and quantitative PCR (qPCR). Clone libraries were constructed to analyze the diversity of 16s rDNA and *mcrA*. Results indicate that the Bangladesh aquifers harbor unique microbial populations. Microbial diversity as determined by T-RFLP indicates that arsenic does not control the microbial diversity. Future plans include enriching for arsenate reducers and examining the distribution of functional genes such as *Arr*. A dozen sediment and water samplers from Bangladesh and from the Vineland site have also been sent for detailed analysis to Duquesne University. Finally, the range of analyses conducted in tubewells of Bangladesh has been expanded to include total coliform and *E. coli* using an EPA-approved method developed by IDEXX (http://www.idexx.com/).

Core D: Hydrogeology Support Laboratory

PI: Martin Stute

Peter Schlosser, Juerg Matter, Steve Chillrud

Progress report

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, and 7, as well as the RTC.

Notable advances for the last period

The main efforts of the Hydrogeology Core laboratory have been focused on preparing for the next round of field work related to our projects 5 and 6. We are planning to trace the geochemical evolution along flow paths from recharge to discharge in Bangladesh and determine how As mobilization would be affected by accidental or purposefully induced changes in groundwater chemistry. We have developed a new drive point sampler with an integrated submersible pump that will allow us to rapidly sample fluids and dissolved gases along vertical profiles from boreholes drilled with local low-tech techniques in Bangladesh. We have also set up and tested a multi-purpose gas chromatograph (funded from another source) for rapid simultaneous measurement of N_2, O_2, Ar, CO_2, CH_4, and H_2 and are currently developing a sampler that separates dissolved gases from water samples in the field. We also supported the design of push-pull and forced gradient experiments in Bangladesh and at the Vineland superfund site by providing modeling capacity and assembling and testing equipment for injections and withdrawals of site groundwater that can be amended with reactive compounds and conservative tracers. These major field experiments will be started in the winter of 2006/07. The routine collection of hydraulic data from monitoring wells and surface waters in Bangladesh has been continuing on a monthly basis.

In support of project 7 we performed in situ tests on community wells in Bangladesh that showed increases in dissolved As concentrations over time and were able to constrain the reasons for the well failure. In collaboration with the NY branch of the USGS and in the framework of the RTC, we collected and measured $^3H/^3He$ samples from 6 wells in Rockland county (NY) to help assess groundwater quantity and quality in this region.

SBRP Training Core

The Training Core will continue its Workshop Program this November with a certification and licensing course on “EPA Lead Paint Inspection and Risk Assessment” given by Dr. Marco Pedone, an expert on hazardous waste management. Besides the monthly Superfund Seminar Series, the Training Core will also again participate in the Annual Granville H. Sewell Distinguished Lecture In Environmental Health Sciences with an invited speaker yet to be announced. Finally, 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:

None

Student Information Updates:

Embedded within test and also updated in attached excel file.