Universidad Autónoma de Chihuahua
Dirección de Planeación y Desarrollo Institucional

Reporte Técnico Parcial del Proyecto

1. Institución u Organismo:

Redes Temáticas de Colaboración académica Convocatoria 2013. PROMEP. SEP.

2. Nombre del proyecto: Consorcio Internacional de investigación en contaminantes ambientales y su efecto en la salud. Exposición ambiental a Arsénico y Diabetes mellitus.

3. No. convenio: OF-13-6894

4. Responsable del proyecto:

Blanca Estela Sánchez Ramírez. No. Empleado 07088 No. De Folio Promep.

Fecha: 15 de diciembre de 2013. 1er. Trimestre.

5. Periodo de vigencia del proyecto: Agosto de 2013 a Julio 2014

6. Reporte de actividades desarrolladas en el proyecto con base en los objetivos y metas: (Descripción detallada, presentar un análisis describiendo cada una de las actividades realizadas en relación al cumplimiento de los objetivos y metas propuestos, incorporar hojas, no más de 3 cuartillas)

7. Descripción de las metas alcanzadas durante el ejercicio del proyecto:

Los objetivos que se contemplaron en este periodo fueron:

1. Seleccionar la población de estudio mediante la aplicación de encuestas de exposición a través de visitas domiciliarias en poblaciones rurales del estado de Chihuahua expuestas a As y F en el agua de consumo.
2. Valorar la fluorosis dental en la población.

1ra. Actividad planteada: Realización a visitas de las poblaciones encontradas con niveles elevados de fluoruros a fin de reclutar participantes para el estudio.

METODOLOGÍA
El diseño del estudio es transversal
Población de estudio:
Se programó trabajar con una población total de 300 personas, distribuidas en tres poblaciones:

- ✓ 100 personas expuestas a concentraciones de fluoruros mayores a 1.5 mg/l.
- ✓ 100 personas expuestas a altas concentraciones de As y fluoruros mayores a 0.05 y 1.5 mg/l respectivamente.

- ✓ 100 personas con valores de As y fluoruros menores o iguales a los permitidos en la norma NOM-127-SSAI-1994 (0.05 y 1.5 mg/l respectivamente).

La selección de las poblaciones se basó en los resultados proporcionados por estudios previos realizados en la Facultad de Ciencias Químicas de la UACh, en la zona de estudio.

Criterios de selección:
Los criterios de inclusión fueron:

1. personas mayores de 18 años que decidieron participar en el estudio y expresaron su voluntad a través de una carta de consentimiento. Se les informó de los objetivos del estudio, los beneficios que recibirán al ser evaluados en su salud a través de una consulta médica y pruebas de laboratorio; la tomas de muestras de sangre y orina que serán necesarias en el transcurso del proyecto, en las que se utilizará material nuevo y estéril; y el compromiso de entregarles de manera personalizada y confidencial los resultados de sus análisis.
2. residencia mayor a 5 años en la comunidad de estudio.
3. Consumir agua de la llave

Los criterios de exclusión fueron:

1. personas que decidieron no participar;
2. menores de 18 años
3. personas que por su trabajo o estudios no residan permanentemente en la comunidad de estudio.
4. Consumo de agua purificada.

Variables a analizar:
Variable independiente: exposición a As y F en el agua de consumo
Variables dependientes: diabetes, obesidad, hipertensión, dislipidemia, fluorosis dental.
Variables confusoras: edad, sexo, antecedentes heredofamiliares, enfermedades renales

Etapas:
Las visitas se realizaron de Julio a Agosto de 2013 en varias etapas, una para cada comunidad involucrada en el estudio, para realizar el procesamiento de las muestras y la entrega de resultados a las personas involucradas.
Cada etapa comprendió:

1. Invitación domiciliaria a participar a los pobladores de las comunidades involucradas en el estudio.
2. Firma de la carta de consentimiento informado
3. Aplicación de entrevista y recolección de muestras de agua de consumo en el domicilio de cada participante.
4. Cita en las unidades médicas de la Secretaría de Salud de cada comunidad. para la toma de muestras, valoración de fluorosis dental y somatometría.
5. Valoración de la fluorosis dental por los médicos odóntólogos participantes en el proyecto.
6. Realización de somatométría y medición de presión arterial
7. Recolección de muestras de orina y toma de muestras de sangre

El instrumento a utilizar para la entrevista, ha sido validado por otros estudios relacionados a la exposición a As en el agua de bebida, realizados por la Dra. Luz María del Razo del CINVESTAV, México, quién participa en el proyecto. La encuesta contiene los siguientes puntos: a) ficha de identificación, b) factores de exposición, c) antecedentes patológicos, d) síntomas no específicos de intoxicación por As y/o Fluoruros, e) tipo de agua de consumo

En las muestras de agua, orina y sangre, se les determinará los siguientes parámetros:
1. Muestras de agua:

A) Determinación de As total por espectrometría de absorción atómica con generación de hidruros (HG-ASS) acoplado a una trampa criogénica para separación de especies arsenicales, en el laboratorio de Analítica III de la FCQ.
B) Determinación de fluoruros por electrodo selectivo de iones en el laboratorio de Biotecnología III de la FCQ.

2. Muestras de sangre:
En el equipo Prestige del laboratorio de Clínicos de la FCQ se realizarán:

A) Química sanguínea: urea, creatinina, ácido úrico y glucosa y fosfatasa alcalina
B) Perfil de lípidos: colesterol-HDL, colesterol, LDL, VLDL, triglicéridos.

3. Muestras de orina:

A) Examen general de orina: análisis fisicoquímico y de sedimento en las unidades médicas en las cuales se realizan los muestreos,
B) Cuantificación de creatinina y ácido úrico en el equipo Prestige del laboratorio de Clínicos de la FCQ

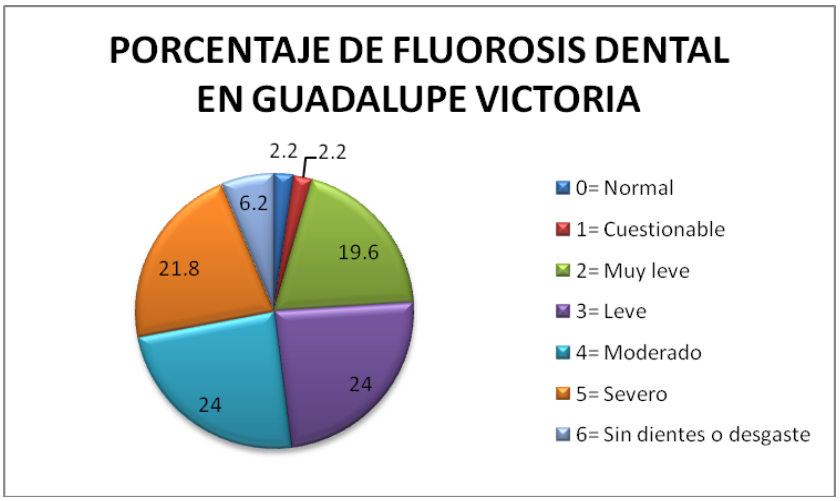
RESULTADOS
IMPACTO SOCIAL

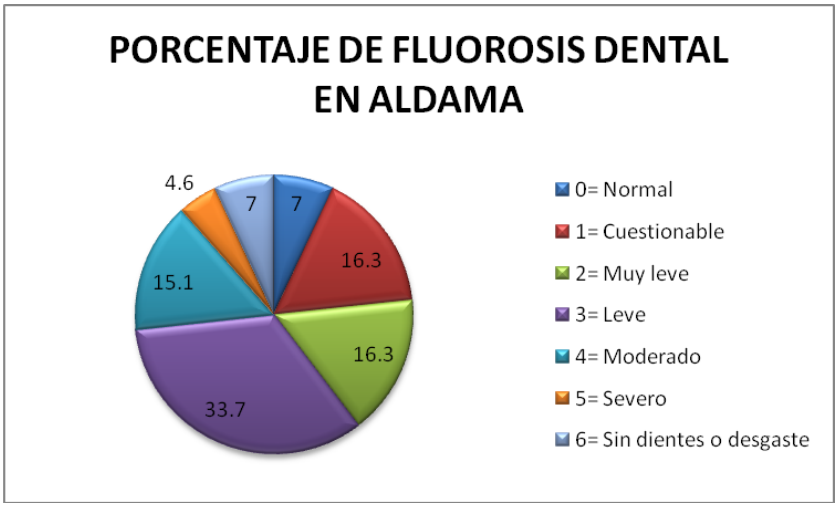
En esta parte del proyecto participaron estudiantes de la Facultad de Ciencias Químicas y de la Facultad de Odontología que en Brigadas de Servicio Social llevaron a cabo la toma de muestras de sangre y orina y la evaluación de fluorosis dental en los participantes. De los 300 participantes propuestos en el diseño, se incluyeron en el estudio un total de 239 participantes que aceptaron participar y que cumplieron con los criterios de inclusión mencionados. La distribución de hombres y mujeres por comunidad se muestra en el Cuadro No. 1.

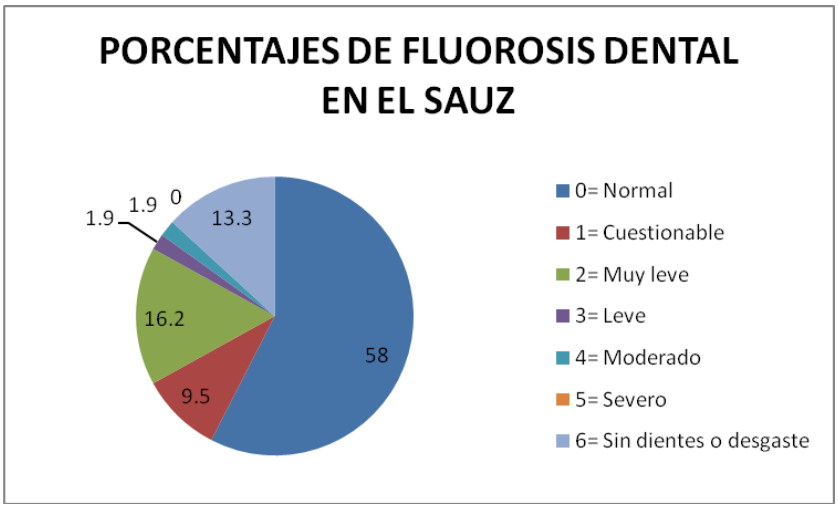
Cuadro 1. Distribución de la población de hombres y mujeres por comunidad

	GUADALUPE VICTORIA (n=46)		**ALDAMA (n=86)**		**EL SAUZ (n=107)**	
	n	%	n	%	n	%
HOMBRES	14	30.5	24	28	30	28
MUJERES	32	69.5	62	72	77	72

Como se muestra en las siguientes gráficas, la frecuencia de fluorosis dental, incluyendo desde muy leve hasta severa fue de 89.4% para la población de Guadalupe Victoria en donde los mayores porcentajes se encuentran con fluorosis leve (24%), moderada (24%) o severa (21.8%). En Aldama el porcentaje total con fluorosis fue de 69.7%, con los mayores porcentajes en fluorosis leve (33.7%); y en la población control de El Sauz fue solo del 20% en total, de los cuales el16.2% presenta fluorosis muy leve, en la mayoría (58%) se encuentra normal.







Están pendientes las actividades relacionadas con los parámetros clínicos así como los valores de As y Fluoruros en orina una vez que se tengan esos resultados y determinar si existe una asociación con la exposición a dichos contaminantes. Estos análisis sr están realizando en el laboratorio de la Dra. Luz María Del Razo en el departamento de Toxicología del CINVESTAV y en el laboratorio de Química Analítica y Biotecnología III de la Facultad de Ciencias Químicas.

8. Productos:

De las actividades realizadas en el primer año del proyecto se obtuvieron resultados que se presentaron en varios foros de difusión científica los cuales se enlistan a continuación:

52va Reunión Anual de la Sociedad Americana de Toxicología. Marzo 10-14 del 2013 San Antonio, Tx, USA

a) Retention of trivalent arsenic metabolites in urothelial cells is associated with markers of As exposure and diabetes.

IX Congreso Nacional de Toxicología SOMTOX 2013. Noviembre 4-9 del 2013. Nuevo Vallarta, Nayarit, Mex.

a) Exposición a arsénico y flúor en comunidades rurales del Edo. de Chihuahua.

ObesityWeek 2013: where science and treatment meet.Noviembre 11-16 del 2013. Atlanta, GA. USA.

a) Moderate Levels of Drinking Water Arsenic Increase Cardiometabolic Risk among Mexican Adults Regardless of Weight Status. Michelle A. Mendez Chapel Hill, NC; Carmen González-Horta, Lourdes Ballinas Casarrubias, Blanca Sánchez-Ramírez, María C. Ishida, Daniela S.Gutiérrez-Torres.
b) B-Vitamins influence arsenic metabolism in Mexico. Michelle A Mendez, Rick Vavolizza, Maria C Gonzalez-Horta, Jesse Saunders, Daniela Gutierrez-Torres, Maria de L Ballinas Casarrubias, Blanca E Sánchez-Ramírez, Maria C Ishida, Luz M Del Razo, Gonzalo Garcia-Vargas, Zuzana Drobna, John Buse, Dana Loomis, Miroslav Styblo. FASEB JOURNAL 27:1077.20

9. Impacto académico:

Los estudiantes del programa académico de Químico Bacteriólogo Parasitólogo involucrados en este proyecto de atención a las comunidades, se integraron en equipos interdisciplinarios con profesionales del área de la salud, como son: médicos, odontólogos, enfermeras e investigadores para atender a las personas que desean participar en este programa.

El aprendizaje basado en proyectos de atención a las comunidades permitirá integrar conocimientos de asignaturas relacionadas y desarrollar competencias específicas de su campo profesional en el área de análisis e interpretación químico-biológica, fomentando así mismo valores de respeto, ética, responsabilidad, servicio a la comunidad y solidaridad

IMPACTO CIENTÍFICO

Se realizó un diagnóstico del efecto que causa a la salud la exposición de manera conjunta al As y Fluoruros en poblaciones rurales del Estado de Chihuahua, tomando como referencia factores de riesgo relacionados con el Síndrome Metabólico como son: obesidad, hipertensión, colesterol, triglicéridos, y analizando su posible relación con la excreción de As y F en orina, como biomarcadores de exposición. Esta información tendrá un impacto científico ya que permitirá analizar el efecto potenciador de As y F en la toxicidad, debido en principio a que no existen reportes que analicen la asociación de dicha exposición, con factores de riesgo del Síndrome Metabólico y por otro lado, debido a que los resultados epidemiológicos del efecto conjunto no son concluyentes. Estos resultados en breve serán publicados en revistas arbitradas internacionales relacionadas con salud y ambiente.

IMPACTO TECNOLÓGICO

Se instaló en la FCQ la metodología apropiada para monitorear y evaluar a poblaciones potencialmente expuestas a As y Fluoruros a través de biomarcadores de exposición y de efecto. Además, es importante mencionar que a través de la colaboración Institucional con el CINVESTAV, mediante la capacitación de estudiantes involucrados en el proyecto, se

implementarán algunas de las metodologías relacionadas con cuantificación de As y F en orina.

10. Actividades de apoyo complementarias:
    a) Registro del proyecto de Maestría en Ciencias de un estudiante involucrado en el proyecto.
    b) Registro del proyecto de un estudiante de licenciatura involucrado en el proyecto.

11. Comentarios adicionales:

Se han estado trabajando varios manuscritos para la publicación de los resultados obtenidos en el proyecto durante el año pasado pero a la fecha siguen en proceso de revisión, se espera que estén aceptados para inicios del año entrante.

Notas: El reporte académico deberá ser remitido en versión magnética por el titular y responsable del proyecto, mediante oficio dirigido al Representante Institucional de Promep el M.A.P. Edel Omar Montoya Maldonado.

Se deberá anexar un ejemplar de la evidencia de los productos obtenidos en el proyecto en el que se incluirá la siguiente leyenda "***Proyecto realizado con financiamiento de la Secretaría de Educación Pública-Subsecretaría de Educación Superior-Dirección General de Educación Superior Universitaria".***

Una vez revisada la información deberá estar disponible en la página electrónica de nuestra Institución.

(*The FASEB Journal*. 2013;27:1077.20)

1077.20

B-vitamins influence arsenic metabolism in Mexico

Michelle A Mendez[1], Rick Vavolizza[1], María C. Gonzalez-Horta[3], Jesse Saunders[1], Daniela Gutiérrez-Torres[3], María de L. Ballinas Casarrubias[3], Blanca E. Sánchez-Ramírez[3], María C. Ishida[3], Luz M. Del Razo[3], Gonzalo García-Vargas[4], Zuzana Drobná[1], John Buse[2], Dana Loomis[5] and Miroslav Styblo[1]

[1] Nutrition, University of North Carolina, Chapel Hill, Chapel Hill, NC
[2] Medicine, University of North Carolina, Chapel Hill, Chapel Hill, NC
[3] 2Universidad Autónoma de Chihuahua, Chihuahua, Mexico
[4] Universidad Juárez del Estado de Durango, Durango, Mexico
[5] IARC, Lyon, France

Little is known about dietary modifiers of health risks from environmental contaminants. Inorganic arsenic (iAs), known to increase risk of several chronic diseases, is metabolized via pathways involving methylation to monomethylarsenic (MAs) and dimethylarsenic (DMAs) prior to excretion. Higher proportions of urinary arsenic as iAs or MAs are thought to increase health risks. Studies in Bangladesh suggesting dietary methyl donors may reduce iAs toxicity by enhancing metabolism have yet to be confirmed in other settings. We explored associations between B-vitamin intakes and urinary As species in 560 adults in Chihuahua, Mexico exposed to iAs in drinking water. In multivariate models, higher dietary folate was associated with a lower proportion of urinary iAs and a higher ratio of MAs to iAs ($P<0.05$), but not with a higher proportion of DMAs. Folate was more strongly associated with lower iAs when vitamin B12 intakes were higher. Findings support that B vitamins influence iAs metabolism, possibly by modulating methyl group availability. Support: NIEHS 5R01 ES015326 -02

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Formato-A1

treatment of HepG2 cells with MMA(V), DMA(V), or TMA(V) alone significantly induces CYP1A1 mRNA, protein, and catalytic activity levels. Furthermore, when the cells were co-exposed to MMA(V), DMA(V), or TMA(V) in the presence of TCDD, there was further potentiation of the TCDD-mediated induction of CYP1A1 mRNA, protein, and catalytic activity levels. In addition, MMA(V), DMA(V), and TMA(V) in the absence and presence of TCDD induced the AhR-dependent XRE-driven luciferase reporter activity, suggesting an AhR-dependent mechanism. In conclusion, this is the first demonstration that As(III) metabolites, MMA(V), DMA(V), and TMA(V) induce CYP1A1 mRNA, protein, and catalytic activity levels in an AhR-dependent mechanism and represents a novel mechanism by which As(III) causes carcinogenicity. Supported by NSERC Discovery Grant RGPIN 250139-12.

PS 2293 Comparative Oxidation State Specific Analysis of Arsenic by High-Performance Liquid Chromatography-Inductively Coupled Plasma-Mass Spectrometry and Hydride Generation-Cryotrapping-Atomic Absorption Spectrometry.

J. Currier[1], R. Saunders[2], L. Ding[2], W.M. Bodnar[3], P. Cable[4], T. Matoušek[5], J. Cosgrif[2] and M. Styblo[2]. [1]*Curriculum in Toxicology, University of North Carolina at Chapel Hill, Chapel Hill, NC;* [2]*Department of Nutrition, University of North Carolina at Chapel Hill, Chapel Hill, NC;* [3]*Department of Environmental Science and Engineering, University of North Carolina at Chapel Hill, Chapel Hill, NC;* [4]*Institute of Analytical Chemistry of the ASCR, Brno, Czech Republic;* [5]*Microbiological and Chemical Exposure Assessment Research Division, NERL, US EPA, Cincinnati, OH.*

Several methods are used for quantifying the toxic inorganic arsenic (iAs) metabolites, methylarsonous acid (MAs^{III}) and dimethylarsinous acid ($DMAs^{III}$), including reversed-phase high-performance liquid chromatography-inductively coupled plasma-mass spectrometry (HPLC-ICP-MS) and hydride generation-cryotrapping-atomic absorption spectrometry (HG-CT-AAS). While HG-CT-AAS has consistently detected these arsenicals in biological samples, HPLC-ICP-MS has provided contradictory results. Here, we compare the capacities of both methods to detect and quantify MAs^{III} and $DMAs^{III}$ in an in vitro methylation system containing recombinant human arsenic (+3 oxidation state) methyltransferase (As3MT), S-adenosyl methionine, a non-thiol reductant tris(2-carboxyethyl)phosphine, and arsenite (iAs^{III}) or MAs^{III} as substrates. HPLC separation of the in vitro methylation mixture resulted in significant loss of MAs^{III} and $DMAs^{III}$ with total arsenic recoveries below 25%. Ultrafiltration showed that both MAs^{III} and $DMAs^{III}$ are bound to As3MT. Oxidation of the mixture with H_2O_2 prior to HPLC separation increased arsenic recoveries to ~95% but oxidized MAs^{III} and $DMAs^{III}$, thus preventing quantification of these metabolites. In contrast, direct HG-CT-AAS analysis revealed large quantities of MAs^{III} and $DMAs^{III}$ and high total arsenic recoveries (>72%) after cysteine treatment. These data suggest that HPLC-ICP-MS can provide false-negative results when used for analysis of MAs^{III} or $DMAs^{III}$ in biological samples containing protein at concentrations as low as those commonly found in human urine.

PS 2294 The Retention of Trivalent Arsenic Metabolites in Urothelial Cells Is Associated with Markers of As Exposure and Diabetes.

M. Styblo[1], J. Currier[1], C. González-Horta[2], L.M. Del Razo[3], B. Sánchez-Ramírez[2], L. Ballinas-Casarrubias[2], G.G. García-Vargas[3], M.C. Ishida[2], R. Saunders[1], Z. Drobna[1] and D. Loomis[4]. [1]*Curriculum in Toxicology, University of North Carolina at Chapel Hill, Chapel Hill, NC;* [2]*Universidad Autónoma de Chihuahua, Chihuahua, Mexico;* [3]*CINVESTAV-IPN, Mexico City, Mexico;* [4]*Universidad Juárez del Estado de Durango, Durango, Mexico;* [5]*University of Nebraska Medical Center, Omaha, NE;* [6]*Department of Nutrition, University of North Carolina at Chapel Hill, Chapel Hill, NC.*

Chronic exposure to inorganic arsenic (iAs) in drinking water has been linked to an increased prevalence of diabetes. Laboratory evidence suggests that methylarsonous acid (MAsIII) and dimethylarsinous acid (DMAsIII) that are formed in the course of iAs metabolism contribute to the diabetogenic effects of iAs exposure. However, no data are available on tissue concentrations of these toxic metabolites in humans. Here, we used a newly developed hydride generation(HG)-cryotrapping(CT)-inductively coupled plasma-mass spectrometry method with limits of detection of 0.04-2 pg As to examine the retention of tri- and pentavalent metabolites of iAs in urinary bladder exfoliated cells (BECs) isolated from urine of 343 residents of Chihuahua, Mexico who ingest drinking water contaminated with up to 400 ppb As. The urinary metabolites of iAs were measured by HG-CT-atomic absorption spectrometry. The sum of As species in BECs ranged from 0.8 to 3,137 pg As/10,000 cells. Notably, iAs was the major species retained in BECs (~60% of total As). MAsIII and DMAsIII accounted for 8 and 2% of total As. We found positive statistically significant correlations between the concentrations of As species in in BECs and in urine ($r = 0.12–0.55$, $p<0.001$). When adjusted for age, sex, and BMI, trivalent arsenicals retained in BECs were significantly correlated with markers of diabetes, fasting plasma glucose (FPG) and 2-hour plasma glucose (2HPG) ($r = 0.13-0.20$, $p < 0.001$). Urinary iAs, MAs, and DMAs also correlated with FPG and 2HPG ($r = 0.15-0.21$, $p<0.001$). Thus, both urinary metabolites of iAs and the metabolites retained in BEC can be used as biomarkers of the diabetogenic effects of iAs exposure.

PS 2295 Oxidation State Specific Analysis of Arsenic Species in Tissues of Wild-type and Arsenic (+3 Oxidation State) Methyltransferase (*As3mt*) Knockout Mice.

C. Douillet[2], J. Currier[1], R. Saunders[2], Z. Drobna[2] and M. Styblo[2]. [1]*Curriculum in Toxicology, University of North Carolina at Chapel Hill, Chapel Hill, NC;* [2]*Department of Nutrition, University of North Carolina at Chapel Hill, Chapel Hill, NC.*

As3mt catalyzes the conversion of inorganic arsenic (iAs) to methylated metabolites, including methylarsonite (MAsIII) and dimethylarsinite (DMAsIII). While this enzyme is critical for the detoxification of ingested iAs, MAsIII and DMAsIII are more toxic than iAs. The *As3mt*-KO mice can thus be used to explore the role of MAsIII and DMAsIII in the adverse effects of iAs exposure. Wild-type (WT) C57BL/6 mice exposed to 50 ppm As as arsenite (iAsIII) in drinking water developed diabetes characterized by impaired glucose tolerance without insulin resistance. Methylated arsenicals were detected in tissues maintaining glucose homeostasis, but the oxidation state of As was not determined. Our recently developed HG-CT-AAS method for the oxidation state specific speciation of As in complex biological matrices was used to compare retention of tri- and pentavalent As species in tissues of WT and *As3mt*-KO mice drinking water with iAs. *As3mt*-KO mice were exposed to 0, 15, 20, 25 or 30 ppm and WT mice to 50 ppm As as iAsIII for 4 weeks. *As3mt*-KO mice retained almost exclusively iAs; iAsIII was the most prevalent species in liver, pancreas, adipose, lung, heart, and kidney, ranging from 53 to 74% of total As. Methylated arsenicals did not exceed 10% of total As in any tissue. Tissues of WT mice retained iAs and methylated arsenicals; iAsIII, MAsIII and DMAsIII represented 55–68% of the total As in the liver, pancreas, and brain. High levels of MAsIII were found in the intestine and intestinal content of WT, but not *As3mt*-KO mice, suggesting that intestinal bacteria are not a major source of methylated As species. Our results indicate that internal total As doses in tissues critical to glucose homeostasis (liver, pancreas, skeletal muscle, adipose) equivalent to WT mice can be achieved in *As3mt*-KO mice after exposure to 25 and 30 ppm As. Future studies will compare the diabetogenic effects of iAs exposure in WT and *As3mt*-KO mice.

PS 2296 Photo-Activatable GFP-Labeled Rat Glucocorticoid Receptor (paGFP-rGR) As Model to Study Effects of Arsenic on Endocrine Receptor Activation and Cellular Localization.

S.K. Schmaling[1,4], F. Zandbergen[1], A. Adebayo[1,2], C.M. Connolly[1,4], V. Chatikavanij[1], J.E. Bodwell[3] and J.W. Hamilton[1,2]. [1]*Marine Biological Laboratory, Woods Hole, MA;* [2]*Brown University, Providence, RI;* [3]*Bridgewater State University, Bridgewater, MA;* [4]*Waldorf State University, Waldorf, RI;* [5]*Dartmouth Medical School, Lebanon, NH.*

Exposure to arsenic (As) is associated with an increased risk of many serious illnesses including several types of cancer, type 2 diabetes, cardiovascular disease, and reproductive and developmental problems. Previous research showed that As can act as an endocrine disruptor, altering the regulation of gene expression by numerous nuclear hormone receptors, including the Glucocorticoid Receptor (GR). At very low doses (0.05-1 μM) As enhanced hormone-mediated, GR-regulated gene expression by 2- to 3-fold. Conversely, at intermediate non-cytotoxic concentrations (1-5 μM) As inhibits receptor-mediated gene expression. We have hypothesized that these differential effects reflect separate mechanisms with different targets and that the inhibited activation could be caused by 1) altered rate of hormone-receptor translocation to the nucleus, 2) altered number of receptors that translocate, 3) altered steady-state nuclear levels of receptor (e.g., by decreases in nuclear export), 4) altered efficiency of receptor function, or some combination of these. To test this, we used HEK293 cells to generate a cell line stably expressing rat GR fused to photo-activatable Green Fluorescent Protein (HEK293-paGFP-rGR), allowing

Abstracts

ance had significant correlation. The adjusted OR (95% CI) for insulin resistance for the lowest vs. highest quartile of house income and education level were 0.66(95% CI 0.55 0.81) and 0.71(95% CI 0.56 0.90) in MODEL1. The adjusted OR (95% CI) for insulin resistance for the lowest vs. highest quartile of house income were 0.71(95% CI 0.56 0.90) in MODEL2. However, such relationship was not found among education level in model2. Conclusions: We found the relationship between SES, especially house income and insulin resistance in non diabetic adult women.

Wednesday, November 13, 2013
Posters on Display: 10:00 AM – 3:30 PM
Location: Exhibit Hall A

Environmental Determinants of Health

T-330-P
Risk of Early Childhood Obesity Associated with Oral Antibiotics and Corticosteroids Administered During Infancy

Charles Bailey, Christopher B. Forrest, Peixin Zhang, Thomas M. Richards, Alice Livshits, Patricia A. DeRusso *Philadelphia, PA*

Background: Medication use early in life has been implicated as a risk factor for obesity, but current evidence is limited. We examined whether exposure to oral antibiotics or steroids at specific times in infancy was associated with early childhood obesity. Methods: We conducted a non concurrent cohort study of 84,679 children in the Children's Hospital of Philadelphia's primary care network. Longitudinal data (2001 2010) were retrieved from the EHR for visits from birth to age 6. Antibiotic, steroid, and ranitidine (negative control) exposures were determined for the first 24 months of life and obesity was defined as a BMI greater or equal to the 95th percentile for age and sex during years 3 5 of life. Cox proportional hazards models were used to estimate the rate ratios (RRs) for the development of obesity. The rate of obesity was examined for those exposed and not exposed while adjusting for demographics, anthropometrics, diagnoses, geographic residence, practice site, and medication exposure. Results: Approximately 68% of children were exposed to antibiotics, 12% to steroids, and 13% to ranitidine in the first 2 years of life. The risk of obesity was associated with antibiotic exposure during the first 6 months of life (RR 1.08; 95% CI:1.02,1.14) and during months 13 18 (RR 1.09; 95% CI:1.04,1.15), and increased with the number of courses of antibiotics. Obesity risk was increased with exposure to steroids in months 13 18 (RR 1.16; 95% CI 1.00, 1.34) but no other time period. A diagnosis of reactive airway disease/bronchiolitis correlated with risk of obesity (RR 1.17; 95% CI 1.12,1.23). The risk of obesity was not associated with ranitidine exposure. Conclusions: Antibiotic and steroid exposures during infancy are each associated with increased risk of developing early childhood obesity, but age at exposure is an important modifier of this risk.

T-331-P
Prolonged Financial Stress Predicts Subsequent Obesity: Results from a Prospective Study of an Australian National Sample

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Background: The body of research investigating socioeconomic inequalities in obesity has paid little attention to the concept of financial stress, which is a direct indicator of economic deprivation. The aim of this research was to assess the effect of prolonged financial stress (FS) on subsequent obesity Methods: Data were from Waves 8 (2008), 9 (2009), and 10 (2010) of Household Income and Labour Dynamics in Australia (HILDA) survey. The outcome was obesity measured in 2010. Prolonged FS was defined as having experienced FS in both 2008 and 2009. FS was measured in each year using seven questionnaire items. Analyses adjusted for health, physical activity, income, education, baseline obesity, and other covariates. Results: Prolonged FS was a strong predictor of subsequent obesity. The adjusted risk of being obese in 2010 were 20% higher (RR: 1.20; 95% CI: 1.10 1.30) among individuals who experienced FS in both 2008 and 2009 than those who did not experience FS in either year. The association of FS with obesity was independent of income and constant across income categories. Conclusions: Obesity prevention research should pay more attention to FS as an important dimension of economic deprivation, a concept that is distinct from common indicators of socioeconomic status such as income. Future research can examine the effect of financial education and counseling programs that help individuals with such skills as money management, budgeting, and saving on a reduction in FS and obesity.

T-332-P
Beyond Single Trees: Random Forests for Characterization of Obesogenic Environments in Children

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Background: Obesogenic environments (OE) have long been hypothesized to be drivers of the obesity epidemic. However, few studies have developed measures to classify OEs empirically. Most studies fragment the study of OEs into separate, thematically distinct variables. The goal of this study was to identify a set of diverse community characteristics that, in combination, characterized OEs. We examined the joint, spatially co occurring distribution of features of the food, land use, physical activity and social environments. Methods: We used random forests, a non parametric machine learning approach, to identify the set of community variables in four domains that best classified OEs. Data were obtained on 1223 communities (census tracts and minor civil divisions) from 37 Pennsylvania counties using multiple data sources. Quartile rank of average body mass index (BMI) z scores (BMI z) at the community level was used to "supervise" the selection of variables. BMI z were obtained from electronic health records of the Geisinger Health System from >160,000 children ages 3 18 years who were geocoded. Obesogenic and obesoprotective communities were defined as the lowest and highest quartiles of the distribution of average BMI z. Results: We identified a set of 15 variables across the four environmental domains that accurately classified 59% of the obesogenic and 70% of the obesoprotective communities ("out of bag" sampling error 35.4%). Conclusions: Obesoprotective environments were identified with greater accuracy suggesting greater heterogeneity in more obesogenic communities. Notably, a 10 year lag in community characteristics provided the best classification results. This has important implications for research and interventions. Random forests offer a new, flexible modeling tool for operationalization of OEs.

T-333-P
Moderate Levels of Drinking Water Arsenic Increase Cardiometabolic Risk among Mexican Adults Regardless of Weight Status

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Background: Growing evidence from experimental and observational studies suggests a number of environmental pollutants contribute to cardiometabolic risk. Arsenic (As) in drinking water has been associated with diabetes. However epidemiologic evidence of a role in other cardiometabolic disorders, atherosclerosis and cardiovascular outcomes, is largely limited to a few studies conducted in highly exposed (water As on the order of 100 ppb), Asian populations in Asia. Methods: Associations between concentrations of As in household drinking water and triglycerides and blood pressure were examined in 928 adults in a cross sectional study in Chihuahua, Mexico in which 75% were overweight/obese. Logistic regression models were adjusted for age, gender, smoking status, alcohol consumer, waist circumference, and BMI. Results: Geometric mean water As was 32.2 vs. 22.5ppb among subjects with vs. without elevated triglycerides (>150µg/dL, 41% of the sample), and 32.8 vs. 25.1ppb among those with vs. without stage 2 hypertension (160/100 or medication use, 23.8% of the sample). Water As was strongly associated with both elevated triglycerides (odds ratio [OR], 95% CI for extreme tertiles 1.5, 1.1 2.2) and hypertension(OR 1.8, 1.1 2.8) after multivariate adjustment. Associations were somewhat stronger among normal weight than obese subjects; excluding those diagnosed with diabetes or hypertension had no meaningful effect. Conclusions: Results suggest exposure to moderate levels of drinking water As may contribute to cardiometabolic risk regardless of weight status. As exposure may help to explain elevated metabolic risk among normal weight subjects.

Memorias

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Formato-A1

EXPOSICIÓN A ARSÉNICO Y FLÚOR EN COMUNIDADES RURALES DEL ESTADO DE CHIHUAHUA, MÉXICO

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La exposición conjunta a Arsénico y Flúor es frecuente porque ambos minerales se encuentran como contaminantes en agua subterránea provenientes de fuentes geológicas. El objetivo fue evaluar la relación entre As y F en agua de consumo y la orina de personas expuestas a través del agua de consumo en poblaciones rurales de Chihuahua, México. En las comunidades en las que se presentan concentraciones altas de As también se encuentran concentraciones altas de F. Se analizó la asociación entre As y F en orina de 600 personas que ingieren agua de la llave. La concentración de As en agua se realizó por espectrofluorometría de absorción atómica y las especies de As en orina se analizaron por cromatografía con trampa criogénica acoplada a espectrometría de absorción atómica. La concentración de fluoruros en agua y orina se midió por potenciometría con electrodo ion selectivo. Las concentraciones de As en agua y orina fueron de 0.1 a 419 ug/L y 5 a 426 ug/L respectivamente. Las concentraciones de fluoruros fueron de 0.01 a 9.9 mg/L en agua y 0.06 a 18.08 mg/L en orina, Se observó una correlación positiva significativa entre As urinario y en agua ($r=2000$; $p<0.0001$) y entre F en agua y orina ($r=0.0878$; $p=0.035$). así mismo, se encontró una correlación positiva entre las concentraciones de As y F en agua ($r=0.8212$; $p<0.0001$), sin embargo la relación entre especies de As y F en orina fue menor ($r=0.1675$; $p<0.0001$), lo cual sugiere que otras fuentes pueden contribuir a la exposición a As y F en estas poblaciones.