Table of Contents	
Emily Carpenter	Evaluation of 1-Nitropyrene as a Surrogate Measure for Diesel Exhaust: Assessment of Personal Air Monitoring Data from an Underground Mine
Stephen Cho	Correlation Analysis of Sleep Study Variables in Obese v. Non-obese Military Personnel Diagnosed with Obstructive Sleep Apnea
Stella Daniels	Assessing the Effects of a Behavior Modification Noise Reduction Program in Hospital Intensive Care Units
Stella Daniels	Occupational Health Nursing Consultation: Small Business Occupational Health Service and Environmental Advocacy
Kat Gregersen	Cost-Effectiveness Analysis of Active-Suspension Driver Seats for King County Metro Buses
Kat Gregersen	Ergonomics in Washington State: Citation Patterns in a Changing Political Climate
Dan Grinnell	Overcoming Literacy and Language Barriers to Improve Safety Knowledge of Washington State Dairy Farm Workers
Kris Hartin	Indoor/Outdoor Particulate Matter Composition in Rural Yunnan Province, China
Erika Keim	Testing Pathogen Reduction in Deployed Composting Toilets
Kristen Kerns	Ambient PCB Concentration Reduction through use of Activated Carbon in the Lower Duwamish Waterway
Meenakshi Kushwaha	Accuracy of Pneumonia Diagnosis for the Cooking and Pneumonia Study: Assessment and Training Plan
Meenakshi Kushwaha	Childhood Lead Exposure in a Vietnamese Battery Recycling Village
Jessica Levasseur	Performance evaluation of a beta version of USEPA's SHEDS-HT chemical exposure model
Grace Liao	Waterborne Paint Exposure in the Auto Body Collision Repair Industry
Julia Marks	Quantifying Chemical Transfer from Fabric to Skin
Trevor Peckham	Dermal absorption of benzo[a]pyrene from soil: Assessment of flux and application to risk assessment of contaminated sites
Joemy Ramsay	Measurement of Urinary 1-Nitropyrene Metabolites as Biomarkers of Exposure to Diesel Exhaust in Underground Miners
Laura Rascón Padilla	Development of an LC-MS/MS Method for the Detection of Halogenated Furanones in Drinking Water
Hee Yon Sohng	Evaluation of employment-related health impact assessments
Catherine Tamaro	Characterization of Organophosphate Pesticides in Urine and Home Environment Dust
Vivian Tran	Hand Massage as a Sponge Processing Method to Characterize Microbes in the Bullitt Center
Julia Weicheld	Influence of Environmental Factors on Mosquito Population Abundance and Distribution in King County, Washington
Margaret Willis	Developing Tools for evaluating and enhancing clinician outreach training on pesticides and child health
Margaret Willis	Exploring clinician training on pesticides and child health and developing curriculum aimed at enhancing self-efficacy
Biostatistics, Epidemologic, and Bioinformatic Training in Environmental Health Trainees (BEBTEH)	
Heather Fowler	Quantitative Microbial Risk Assessment of salmonellosis for owners of backyard poultry flocks, Seattle, WA
Karen Hinckley Stukovsky	Estimating Average Ambient Air Pollution Exposure across Zip Codes: A Simulation Study
Jun Hwang	Instrumental Variables for Survival Models with Endogenous Regressors
Joshua Keller	Covariate-adaptive Clustering of Exposures for Air Pollution Epidemiology Cohorts
Erin Riley	Black carbon and ultrafine particle counts downwind of two major airports
David Scoville	Heterogeneity in Quantum Dot Induced Lung Inflammation and Toxicity in Recombinant Inbred Mouse Strains from the Collaborative Cross
Ian Stanaway	The Population Oral Microbiome of Individuals Living in a Farming Community Reveals an Agricultural Oral Microbiome Signal
Gillian Tarr	Using Phylogenetics to Better Understand the Epidemiology of Escherichia coli O157: Methods and Conceptual Framework
Whitney David	Inference following adaptively designed group sequential studies
Sheldwin Yazzie	Assessing Indoor Radon Exposure on the Navajo Nation

The following abstracts are from the 2nd year Master of Science and Master of Public Health degree students in our Environmental Health, Occupational and Environmental Medicine, Occupational and Environmental Exposure Science, Toxicology, and Environmental and Occupational Health programs.

Evaluation of 1-Nitropyrene as a Surrogate Measure for Diesel Exhaust: Assessment of Personal Air Monitoring Data from an Underground Mine

Emily Carpenter
Occupational and Environmental Exposure Science, MS
Preceptor: Christopher Simpson

Objectives: We will investigate the hypothesis that 1-Nitropyrene (1-NP) concentration in air is a viable surrogate measure of diesel exhaust exposure, as compared with industry-standard elemental carbon (EC) and total carbon (TC) measurements. 1-NP content in personal air samples was measured for a cohort of underground miners and compared with measures of Elemental Carbon (EC), Organic Carbon (OC), and Total Carbon (TC) in the same samples.

Methods: Personal exposure data were collected on a cohort of 20 employees at a large underground metal mine during 4 different sample campaigns. Full-shift personal sampling was conducted using both an MSHA compliant SKC DPM impactor downstream of a GS-1 cyclone pre-filter, and a PTFE filter downstream of a GS-3 cyclone. Each DPM filter element was analyzed for EC and OC using NIOSH method 5040. Each PTFE filter was extracted with methylene chloride and analyzed for 1-NP using an LC/MS/MS method. Additionally, after EC and OC analysis each DPM filter was extracted with methylene chloride and analyzed for 1-NP using the LC/MS/MS method.

Results: 1-NP analysis of data from nine cascade impactors indicates that the smallest size fraction of particles, <0.25 µm, contains a majority of 1-NP mass (90% average). Regression analysis of 1-NP vs. EC yields an 8.7% increase in geometric mean (GM) 1-NP for each 10% increase in GM EC ($p<0.001$), and a 10.9% and 13.3% increase in GM 1-NP per 10% increase in GM OC and TC ($p=0.007$ & $p<0.001$, respectively).

Conclusions: 1-NP is found primarily in the respirable particles <0.25 µm, consistent with the known size distribution of diesel exhaust particles. The MSHA compliant SKC DPM impactor has a cut-point of 0.8 µm, and is expected to capture the majority of 1-NP-containing particles present in the mine. Additionally, 1-NP was found to be associated with EC, OC, and TC in personal air samples.

Correlation Analysis of Sleep Study Variables in Obese v. Non-obese Military Personnel Diagnosed with Obstructive Sleep Apnea

Stephen Cho
Occupational and Environmental Medicine, MPH
Preceptor: Debra Cherry

Abstract: Background/Introduction: Several studies have established an association between obesity and Obstructive Sleep Apnea (OSA), but the exact mechanism of interactions remains unknown. Military records offer an opportunity to compare OSA in obese and non-obese patients in order to further characterize the relationship between obesity and OSA, since high number of non-obese soldiers undergoes sleep studies due to unique culture of military medicine.

Methods: Our cross-sectional study explores different associations of diagnostic markers of OSA with selected physiologic sleep disturbances among obese (body mass index (BMI) ≥ 30 kg/ m2) and non-obese (BMI < 30 kg/ m2) patients with OSA. We reviewed and analyzed a database of OSA cases (N=342) comprised of soldiers diagnosed with OSA who underwent polysomnography (PSG) at a major military medical center in 2010. The cases were divided into obese (n= 176; body mass index (BMI) ≥ 30kg/m2) and non-obese (n=166; BMI <30kg/m2). Pearson correlations (r) were calculated for Apnea Hypopnea Index (AHI) among patients with mild OSA (5 ≤ AHI < 15), moderate/severe OSA (AHI ≥ 15), and both groups combined. PSG variables (arousal index, minimum oxygen saturation (O2 Sat)) were compared between the obese and non-obese groups.

Results: A statistically significant correlation between AHI and AI was only seen in moderate-severe OSA for obese patients ($r = 0.55$, $p < 0.01$) while significant correlations were seen in both mild ($r=0.20$, $p=0.02$) and moderate-severe OSA ($r = 0.45$, $p < 0.01$) for non-obese patients. On the other hand, statistically significant correlations between AHI and min O2 were found in both mild ($r=-0.37$, $p<0.01$) and moderate-severe ($r = -0.38$, $p < 0.01$) OSA for obese patients while the correlation was only found in mild($r = -0.26$, $p = 0.01$) OSA for non-obese patients. Furthermore, the correlation between AHI (≥5, without a disease severity stratification) and min O2 sat was significantly (more than twofold) stronger for obese ($r = -0.56$, $p < .01$) than for non-obese patients ($r = -0.27$, $p < 0.01$) and the difference was also statistically significant ($p < 0.01$).

Conclusions: Results suggest that obstructive events during sleep in non-obese and obese patients with OSA might involve and even trigger different cascades of pathophysiologic events. The correlation between frequency of arousal (AI) and number of obstructive events (AHI) increases as the disease progresses and the depth of hypoxia was consistently associated with the number of obstructive events throughout the disease severity for obese OSA patients. However, although, the correlations between frequency of arousal and number of obstructive events also increases as the disease gets more severe, they were losing association between the number of obstructive events and the depth of hypoxia as disease gets worse. Given that physiologic disturbances from the primary pathologic event of OSA may differ as a function of obesity, future study should focus on clarifying the different clinical manifestations of OSA in obese and non-obese patients and may further consider comparing the efficacy of treatment(s) for OSA between obese and non-obese patient groups.

Assessing the Effects of a Behavior Modification Noise Reduction Program in Hospital Intensive Care Units

Stella Daniels
Environmental and Occupational Health, MPH
Preceptor: Noah Seixas

Background: In the intensive care unit (ICU) setting, physiological monitoring and general noise contributes to fragmented sleep in critically ill patients, increasing the risk for sleep deprivation. An environment that increases the risk of sleep deprivation could lead to long-term health consequences especially for the critically ill.

The University of Washington Medical Center (UWMC) 5E and 5SE ICUs implemented noise reduction behavior modification interventions among the nursing staff in three phases. Phase 1 (January 2013) included engagement of key stakeholders, addressing monitor alarms, instituting "Quiet Times" (2-4pm and 10pm-6am), decreasing noise associated with phones, overhead paging, and modifying equipment (e. g., padding the pneumatic tube system). Phase 2 (May 2013) involved installing noise meters throughout ICU locations, and training "Super-Users" to train peers on tailoring alarms for physiological monitoring equipment. And, Phase 3 (November and December 2014) reinforced previous interventions, identified a "Champion" in one ICU, encouraged the nursing staff to be creative, and share successful sleep promoting interventions.

Objective: The objective of this project was to assess the effectiveness of Phase 3 interventions executed in UWMC's 5E and 5SE ICUs to characterize the sound levels to which patients are likely exposed.

Methods: Noise dosimeters recorded sound levels for four 24-hour periods in 10 designated patient rooms, irrespective of a patient, before and after Phase 3.

The mean and standard deviation describes the sound levels in the two units by before and after Phase 3, specific time frames and the rooms. The fraction exceeding 55 decibels (dB) and the 90th percentile of the estimated Leq, and the fraction of exceedance above the moving average at the 5, 10 and 15 dB levels describes the amount of variability observed. A two-sample t-test tested the pre and post intervention sound levels for significance.

Results: Preliminary results show on 5E a pre-intervention mean of 53.1, post-intervention mean of 51.4, with a 95% CI of 1.68 – 1.76, (p-value <0.001) and on 5SE a pre-intervention mean of 55.7, post-intervention mean of 55.3, with a 95% CI of 0.40 – 0.48, (p-value <0.001).

Conclusion: Phase 3 behavior modification interventions employed in the 5E and 5SE ICUs resulted in a statistically significant decrease in noise levels. The effectiveness of the noise reduction interventions is supported by objective measures and offers promising avenues to creating a more restful and rehabilitative environment in ICU settings.

Occupational Health Nursing Consultation: Small Business Occupational Health Service and Environmental Advocacy

Stella Daniels
Environmental and Occupational Health, MPH
Preceptor: Butch de Castro

Issues: Small businesses are less likely to seek occupational safety and health services due to economic factors; therefore, the risk of work-related injury is higher for workers in such settings. Generally, registered nurses lack awareness of the legislative process to advocate for significant legislative initiatives relevant to health, particularly occupational and environmental health.

Description: This project comprised of consulting services for a company engaged in ship repair and restoration services to review their current Safety and Health Manual, updated their respiratory protection program, and provided recommendation(s) for low cost hearing conservation program providers. Law enforcement workers were provided their annual health and safety training, including medical clearance for respirator fit testing, performing respirator fit testing, and "just-in-time" health education topics chosen by the workers.

For the second issue, observation and participation in advocacy work with a coalition of various organizations to re-introduced the bill to ban flame-retardants in consumer products.

Lessons Learned: Small businesses require balancing occupational health services and economical needs of the company. An occupational health consulting company flexible in charges and class content for example, can easily meet the small business' needs to provide safety and health training to workers. As for advocacy, networking, affiliations and partnerships are key to formulate a strong stance on an issue.

Recommendation: Increase awareness of the no-cost consulting services at the Department of Labor & Industries (L&I) and the Field Research and Consulting Group (FRCG) at the University of Washington, Department of Environmental and Occupational Health Services. Next steps include: (1) a descriptive study to evaluate employer awareness of these options, (2) development of a continuing education course targeting a nurse audience increasing awareness about the legislative process, with emphasis on occupational and environmental health related policy initiatives is a key step for advancing nurses' ability to participate in policy advocacy.

Cost-Effectiveness Analysis of Active-Suspension Driver Seats for King County Metro Buses

Kat Gregersen
Environmental and Occupational Health, MPH
Preceptor: Peter Johnson

Low back pain (LBP) is a leading cause of occupational disability and a large contributor to worker compensation costs among bus drivers at King County Metro, the public transit entity in Seattle. LBP in drivers is associated with whole body vibration (WBV) exposures that occur during daily driving. To counteract WBV exposures, engineering controls such as improved seats for drivers may be used. One recently designed seat incorporates active-suspension technology but is more costly than other bus driver seats on the market. This study used a Markov model and cost-utility analysis to determine whether active suspension bus driver seats would be a cost-effective seating alternative to prevent LBP among King County Metro drivers. To determine cost-effectiveness the worker compensation claim database from 1999-2013 for King County Metro was obtained. Back claims were classified with regard to their likelihood of WBV-relatedness and severity. Expected reductions in claim rates were determined from previous research on the Metro driver population and from other interventions targeting LBP in drivers. Quality of life estimates for back pain were acquired from the health-related quality of life literature. Preliminary results suggest that if King County Metro were to install active-suspension driver seats, the agency would improve driver health and potentially reduce costs. The recent engineering advances in driver seat technology may benefit Metro's bottom line in addition to improving driver health.

Ergonomics in Washington State: Citation Patterns in a Changing Political Climate

Kat Gregersen
Environmental and Occupational Health, MPH
Preceptor: Bill Daniell

Overcoming Literacy and Language Barriers to Improve Safety Knowledge of Washington State Dairy Farm Workers

Dan Grinnell
Occupational and Environmental Exposure Science, MS
Preceptor: Michael Yost

AIMS: The goals of this project were to evaluate the effectiveness of a method for reporting biomonitoring results to Latino dairy farm workers as well as provide an annotated list of workplace health and safety training resources for Washington dairy farms. As shown in previous studies, an increasing number of US dairy farm workers are foreign born, are unable to read or speak English, and have limited formal education. Communicating with this large, diverse, and often transient population of workers is challenging.

METHODS: This report describes the development, implementation, and evaluation of a strategy for conveying the potential health risks associated with pyrethroid pesticide metabolite concentrations in urine samples collected from dairy workers on a farm in Washington State. The communication strategy was developed in collaboration with research staff familiar with the dairy workers and was implemented during individual one on one meetings with study participants. Using visual displays of information, key messages were conveyed regarding personal pyrethroid exposure and health risk which were compared to exposure levels found in Latinos of the general population in Washington state. Post-meeting questionnaires qualitatively assessed workers' knowledge of pyrethroid pesticides, pesticide exposure reductions methods and health risks associated with pyrethroid metabolite concentrations found in urine. Finally, an annotated list of resources addressing common workplace injuries and sources of injuries affecting Washington state dairy workers was created based on a review of 1,851 workers compensation claims provided by the Washington State Department of Labor and Industries SHARP program.

KEY FINDINGS: Follow -up questionnaires revealed that workers understood some of the main routes of exposure to pyrethroid pesticides as well as several exposure reduction methods. Diagrams using proportionally sized circles representing participant pyrethroid metabolite urine concentrations and the 95th percentile of pyrethroid metabolite urine concentrations for the Washington Latino population, effectively conveyed personal exposure results and their health implications. From 2009 to 2013, Washington state dairy workers had a higher average injury claim rate (2.61 claims per 100 FTEs) compared to all Washington workers (1.51 per 100 FTEs). The most frequent injuries were sprains, strains, and tears (23.97% of total claims). The most frequent source of injuries were cattle (33.59% of total claims) which caused injury most frequently during an assault by the animal (20.96% of total claims).

CONCLUSION: This risk communication experience indicates that it is possible to adequately convey complex scientific findings in a way that is useful and accessible to those without English language proficiency or much formal education. Careful evaluation of different approaches to risk communication can be effective in identifying communication strategies that produce the greatest comprehension of information and produce health-promoting action by workers. Finally, dairy farm workplace health and safety training efforts should focus on safety hazards created by animals (cattle) in order to prevent injuries such as sprains, strains, and tears as well as bruises and contusions most frequently suffered by dairy workers from 2009 to 2013.

Indoor/Outdoor Particulate Matter Composition in Rural Yunnan Province, China

Kris Hartin
Occupational and Environmental Exposure Science, MS
Preceptor: Edmund Seto

Background: Exposure to high concentrations of fine particulate matter air pollution, with mean diameter of 2.5 micrometers or less (PM2.5), is associated with a range of adverse health effects from birth outcomes to lung cancer. The source (composition) and concentration of the PM2.5 influence the prevalence and severity of these health effects. Exposure to PM2.5 is a function of both the background pollution in a community, and the activities of the individual. In rural China biomass and coal are commonly used for cooking and heating. The incomplete combustion of these fuels raise the concentration of PM2.5, and emit other potentially harmful gaseous byproducts. In Xuanwei, an area of rural Quijing Prefecture in northern Yunnan Province, China, rates of lung cancer are several times higher than the national average. Since the area is not known to be unique in its fuel use and exposure to PM2.5, more research is needed to elucidate the relationship between exposures to air pollution and health outcomes. The composition of the PM2.5 air pollution both within and outside of households in this area may improve understanding of the sources of air pollution and the levels to which individuals may be exposed.

Objective: The objective of this pilot study was to assess the indoor and outdoor PM2.5 concentration and composition of nine residences in rural Yunan province, China.

Methods: Concurrent 12 and 24-hour indoor and outdoor PM2.5 gravimetric samples were collected on Teflon filters in three villages in rural Yunnan province, China in July 2014. Three households in each the villages were sampled. The filters were analyzed for mass concentration, metals and particle bound polycyclic aromatic hydrocarbons (PAHs).

Results: Analysis is ongoing, but preliminary results show a 100 fold difference in concentrations amongst the indoor samples from 23 to 2263 μm/m3, indicating a marked difference in potential exposure to fine particle air pollution. Outdoor concentrations were less variable with a range from 16 to 25μm/m3. Quantifiable results for several PAHs, including 1-nitropyrene and levoglucosan, and metals including lead, arsenic, and bromium was found. These preliminary results suggest that exposures to high concentrations of fine particulate air pollution is still occurring in this area of rural China. Further, the composition of this air pollution may contain harmful constituents that are exacerbating the adverse health outcomes. Additional studies are needed to adequately assess this relationship.

Testing Pathogen Reduction in Deployed Composting Toilets

Erika Keim
Environmental Health, MS
Preceptor: Scott Meschke

Pathogen transmission is a major concern when implementing sanitation systems in resource poor areas. Multiple studies have shown that ecological sanitation systems are an effective means for improving health in areas where standard systems cannot reach disparate populations. Emerging designs of ecological sanitation systems provide needed access to hygiene but they still require confirmation of their effectiveness in reducing pathogen loads in the waste and transmission of disease. A novel composting toilet design is being tested using an auger system to mix and transport feces and a cover material in an attempt to incorporate critical elements to accelerate pathogen die off. Test units have proven to be popular among recipients. This highly economical composting system has been successfully deployed into 11 different communities with a total of 98 toilets in Ecuador that previously had no improved sanitation options. A subset of active composting toilets were monitored for 2 months, taking samples at different points in the treatment line to determine the presence and quantity of total coliforms, E.coli, helminth ova and Salmonella spp. Samples were used to determine pathogen die-off through the treatment line according to time, pH, temperature and moisture content. Using linear regression extrapolation we found that total coliforms and E.coli reduction were primarily dependent on compost storage time. Treatment within the reaction chamber and other environmental factors did not significantly contribute to indicator reduction. Treated compost directly out of the reaction tube showed minimal reductions in indicator levels, and were above acceptable delineated by EPA biosolids class B and WHO guidelines for reuse in agriculture. However, significant reductions were found after being stored for varied periods of time, as recommended by system developers. Some Helminthes were also present in the treatment line and at some endpoints for some of the study's toilets. Salmonella spp. were not found in samples throughout the treatment line. Under the current deployment and usage practices, these composting toilets will require additional treatment and extended storage time prior to beneficial use of the compost as a soil amendment. Further development of the technology to improve environmental conditions in the treatment line could change pathogen survival patterns and corresponding recommendations for compost use.

Ambient PCB Concentration Reduction through use of Activated Carbon in the Lower Duwamish Waterway

Kristen Kerns
Environmental Health, MS
Preceptor: John Kissel

Decades of industrial activity along the Lower Duwamish Waterway have resulted in significant pollution of the sediments, water, and aquatic life in the area. Through the U. S. Environmental Protection Agency's Superfund Program, the Lower Duwamish Waterway is being remediated for numerous Contaminants of Concern, including Polychlorinated Biphenyls (PCBs). The Record of Decision, published in November 2014, identified enhanced natural recovery as one remedial technology slated for implementation to help reduce dissolved (and therefore bioavailable) concentrations of contaminants in the waterway through sequestration. As part of the implementation, activated carbon is proposed as an amendment to enhanced natural recovery pending the results of design phase pilot testing. A hydrophobic organic contaminant mass transfer model, developed by Luthy and Cho, was utilized to predict PCB concentration reductions in sediment pore water for three PCB congeners. The model relied upon a series of parameters specific to sediment characteristics, properties of the activated carbon, and kinetic characteristics specific to the PCB congener modeled. A combination of Lower Duwamish Waterway specific parameters and default parameters set in the model were used. Model results predicted a 68% reduction in PCB 180 concentrations over a one year period under the most probable scenario for activated carbon. A maximum reduction of 96% and minimum reduction of 8% were also estimated, depending upon the specific input parameters assumed for the model. Similar reductions were predicted for the PCB 153 and PCB 101 congeners. The mass transfer model was then applied to field data from Puget Sound Naval Shipyard, another sediment site with PCB contamination where activated carbon was placed in 2012 as part of remedial efforts at the site. Results from the model were compared to actual concentration reductions seen at Puget Sound Naval Shipyard at the ten month post construction period. The model predicted a PCB 180 concentration reduction of 62%, which falls within the 95% confidence interval of measured reduction seen at the site. However, model results for PCB 153 and 101 over predicted actual reductions and the prediction for PCB 101 fell outside the 95% confidence interval of the observed mean result. The results of this predictive modeling have implications for remedy implementation in the Lower Duwamish Waterway.

Accuracy of Pneumonia Diagnosis for the Cooking and Pneumonia Study: Assessment and Training Plan

Meenakshi Kushwaha
Environmental and Occupational Health, MPH
Preceptor: Deborah Havens

Indoor air pollution from open fires and leaky stoves is a major threat to health, ranking 10th in the WHO comparative risk assessment for the global burden of disease. Malawi has the highest rates of death among infants and children under 5 deaths with pneumonia being the leading cause of childhood mortality.

The objective of the Cooking and Pneumonia Study (CAPS) is to determine whether an advanced cookstove intervention that reduces biomass smoke exposure can prevent pneumonia in children aged younger than 5 years in Malawi. Physicians use the WHO IMCI pneumonia assessment protocol for diagnosis which is the primary outcome of the study. Successful study implementation therefore relies on accuracy of childhood pneumonia diagnosed by clinical staff.

The aim of this project was to develop knowledge assessment tools in order to determine whether the IMCI criteria for pneumonia has been successfully taught to the health workers, how compliant they are with using the criteria and if they are not compliant, to get a better sense of why. This assessment plan includes a mix of survey questions and observation to better understand the lack of compliance. Evaluations will be done at both project sites. In order to ensure inter-observer reliability, the clinical officers will perform few evaluations simultaneously (on the same subject) until they reach at least 90% match in their evaluations. In addition, a training plan was made after consultation with clinical officers from both study sites (Chikwawa and Chilumba). There is emphasis on group activity and problem solving.

Childhood Lead Exposure in a Vietnamese Battery Recycling Village

Meenakshi Kushwaha
Environmental and Occupational Health, MPH
Preceptor: Bill Daniell

Background: Battery recycling and manufacturing are major sources of occupational exposure to lead. Residents of Dong Mai village in northern Vietnam have been involved in battery recycling since the 1970s. To address pervasive lead contamination a remediation plan was developed by Blacksmith Institute in collaboration with Vietnamese national and local authorities. This is an ongoing study with the primary aim of determining changes in child lead exposures after lead remediation activities and a secondary aim of identifying risk factors for childhood lead exposure.

Methods: All children in the village 6 years of age and younger were eligible and invited to participate in the study. A total of 250 children participated in baseline measurements in December 2013; 209 of the 250 children participated in follow-up assessment in September 2014. Written informed consent was collected from parents/guardians of participants. Parents or guardians of participants also responded to interviewer-administered household survey on involvement in recycling activities, use of personal protective equipment, and personal hygiene of household members including children. For data analysis BLL was categorized based on U.S. CDC recommendations for treatment (≥45 μg/dL). Higher values were split based on the instrument measurement limit (>65 and 45-65 μg/dL) and lower values were split into two categories of approximately equal size (10-19 and 20-44 μg/dL). Bivariate analysis was conducted between categorized BLL and covariates using chi-square, Fisher exact tests, or one-way ANOVA.

Findings: At baseline, all children tested with Lead Care II had elevated BLLs : 24% had BLL >65 μg/dL; other values had mean 35.2 μg/dl (sd 11.5), with lowest value, 6.9 μg/dL. Current recycling at home, involvement of household members in recycling, duration of home-based recycling activities, and proximity to a recycling operation were all significantly associated with very high BLLs. Time spent by child in outdoor environment was also significantly associated with very high BLLs. At the follow-up assessment BLLs displayed a downward trend: >65 (5% follow-up versus 24% baseline), 45-65 (11% versus 17%), 20-44 (56% vs 53%), and 10-19 (26 % vs 6%).

Interpretations: Follow-up BLLs, though still high, point towards favorable impact of lead remediation activities in Dong Mai village. However, this study evaluates remediation activities in only one village. We do not have a control group for external comparison, but we consider this unlikely to be a secular trend.

Funding: Fogarty International Center/NIH D43 TW000642; and Rohm & Haas University of Washington Professorship in Public Health Sciences.

Performance evaluation of a beta version of USEPA's SHEDS-HT chemical exposure model

Jessica Levasseur
Environmental Health, MS
Preceptor: John Kissel

The United States Environmental Protection Agency (USEPA) is in the process of developing a high throughput (HT) model for exposure-based prioritization in the ExpoCast program to inform toxicity testing and chemical risk assessment. This mechanistic modeling approach is adapted from the prior Stochastic Human Exposure and Dose Simulation (SHEDS) framework, which was implemented in SAS. SHEDS-HT, written in R, reduces user burden and input demands by linking chemicals to particular exposure scenarios based on consumer product categories or food groups. SHEDS-HT rapidly generates probabilistic population distribution estimates of pathway-specific exposures, overall exposures, and intake doses. These predictions are based on particular exposure scenarios, a fugacity-based indoor environmental media model, and information from human activity databases. The predictive ability of SHEDS-HT is best evaluated by comparison to available biomarker measurements or to alternative predictions from prior measurement-intensive exposure studies. A key example of the latter is the USEPA Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP) study, which was conducted in Ohio and North Carolina. CTEPP provides both environmental and corresponding urinary biomarker data for a relatively large sample of commonly encountered commercial chemicals. NHANES also provides representative urinary biomarker data for some of the same compounds on a whole US population basis. However, biomarker data can reflect both exposure to a parent compound and direct exposure to its biomarker. Absence of environmental measurements for most biomarkers greatly reduces the number of compounds for which complete accounting for inputs and outputs can be conducted. In this evaluation of SHEDS-HT, focus is placed on 2,4-dichlorophenoxyacetic acid (2,4-D) and the parent compounds of the urinary biomarker 3,5,6-trichloro-2-pyridinol (TCPy), which include chlorpyrifos, chlorpyrifos methyl, and triclopyr.

Waterborne Paint Exposure in the Auto Body Collision Repair Industry

Grace Liao
Occupational and Environmental Exposure Science, MS
Preceptor: Noah Seixas

Objectives: The purpose of this study was to characterize workers' exposure to emerging waterborne coatings used in automotive refinishing systems and observe other work practices associated with using these products.

Methods: Ten auto body shops in King County, Washington that use waterborne coatings were recruited to participate in this study. Based on reviews of MSDSs, 14 target compounds were selected to characterize exposures to components of waterborne basecoats. Task-based personal air sampling was conducted on 11 painters when applying basecoats. Samples were collected at 100 and 400 ml/min, an attempt to achieve the limit of detection of sorbent tubes and prevent analyte breakthroughs. Sampling results were summarized and compared to MSDSs and historical exposure studies of solvent-based paints. Painters' work practices were also recorded to determine other possible routes of exposure. Work practices recorded included the use of PPE, gun-cleaning procedures, waste disposal, and paint booth maintenance.

Results: Breathing zone concentrations of aromatic hydrocarbons and polar volatile organic compounds were typically below their respective method limits of quantitation (MLOQ). On average 11% (SD= 16%) of the aromatic hydrocarbon samples and 23% (SD=19%) of the polar compound samples exceeded their respective MLOQs. All analyte concentrations had threshold limit value (TLV) parametric exceedance fractions below 0.03, and had National Institute of Occupational Safety and Health (NIOSH) odor parametric exceedance fraction below 0.05. VOC exposure levels when spraying wateroborne painter were 5 to 72 times higher than historical studies on VOC exposures to solvent-based paints. Procedures for cleaning paint guns and disposing of waterborne paint wastes varied between shops. Several shops disposed of waste in the municipal solid waste stream without chemical characterization, in violation of state regulations. Painters were observed using lacquer thinner to clean their waterborne paint guns, which is not recommended by manufacturers. Painters were also observed handling waterborne waste with inadequate exposure control. We observed that the flow rates in spray booths typically failed to meet OSHA requirements.

Conclusions: Workers' exposures to target compounds when applying waterborne basecoats were typically below their respective MLOQs and regulatory limits. The levels were also lower than the historical exposure levels of spraying solvent-based paints. However, without maintaining adequate airflow in the paint booths adequate guidelines on all aspects of handling the paints, workers can still be at risk to different routes of hazardous exposures. Therefore, more information is needed on the chemical composition of the waste generated from waterborne paint systems to establish best practices for spray gun cleaning and waste disposal.

Quantifying Chemical Transfer from Fabric to Skin

Julia Marks
Environmental Health, MS
Preceptor: John Kissel

Many commercial textiles (clothing, linens, upholstery, furniture) are impregnated, or may be contaminated with, chemicals capable of penetrating the skin. Several researchers have detected high concentrations of metals, pesticides, flame-retardants, phthalates, and optical brighteners in children and adult clothing items. Other studies have demonstrated the transmission of chemicals from clothing to urine. However, the fabric-to-skin pathway remains poorly quantified. This study aims to measure the rate at which a low volatility optical brightener would transfer from clothing to and through the skin. [14C]-7-hydroxycoumarin was applied to three types of fabrics in two fabric concentrations. Human cadaver skin was exposed to the loaded fabric in vitro for 24-hours. Migration of the radiolabeled compound was measured by liquid scintillation counting (LSC). Data produced by this study enabled the calculation of flux to skin (ng/cm2/hr) as well as a fabric-specific mass transfer coefficient (kF). Analysis of the data suggests that dermal exposure to chemicals in textiles can contribute to the total body burden of such compounds. Quantification of fabric-to-skin transfer rates can aid in the assessment of the effects of fabric type, fabric load, and contact time on chronic exposure to semi-volatile organic chemicals.

Dermal absorption of benzo[a]pyrene from soil: Assessment of flux and application to risk assessment of contaminated sites

Trevor Peckham
Environmental Health, MS
Preceptor: John Kissel

In vitro assessments of 14C-benzo[a]pyrene (BaP) absorption through human epidermis were conducted with the sub-63-µm fraction of four test soils, containing different amounts of organic and black carbon. Soils were artificially weathered and applied to epidermis at BaP concentrations of 3 and 10 mg/kg for 8 or 24 h. Experiments were also conducted at 24 h with unweathered soils and with BaP deposited onto skin from acetone at a comparable chemical load. For the weathered soils, absorption was independent of the amount of organic or black carbon, the mass in the receptor fluid was proportional to exposure duration but independent of concentration, and the mass recovered in the skin after washing was proportional to concentration and independent of exposure time. Results from the weathered and unweathered soils were similar except for the mass recovered in the washed skin, which was lower for only the higher concentration by less than 50%. The findings are consistent with concentrations that exceeded the BaP sorption capacity of all soils tested, and with BaP mass in the wash skin dominated by particles that were not removed by washing. Flux into and through skin from soils were lower by an order of magnitude from acetone-deposited BaP.

Measurement of Urinary 1-Nitropyrene Metabolites as Biomarkers of Exposure to Diesel Exhaust in Underground Miners

Joemy Ramsay
Occupational and Environmental Exposure Science, MS
Preceptor: Christopher Simpson

Exposure to diesel exhaust (DE) is common in occupational and environmental settings and has been associated with several adverse health outcomes. Therefore, the ability to accurately quantify DE levels is crucial for understanding and controlling exposures. A DE-specific chemical component, 1-Nitropyrene (1-NP), has been proposed as a potential marker for exposure to DE in air and biological samples. In this study the suitability of 1-NP urinary metabolites as biomarkers for monitoring occupational exposure to DE was evaluated. The study took place in a large underground metal mine that uses diesel engines extensively. Air and urine samples were collected from a cohort of 20 miners who performed a variety of jobs located within the mine. Four sampling campaigns were conducted, each 2-3 months apart. During each campaign personal air samples, pre- and post-shift urine, and job task/activity surveys were collected for each subject. Air samples (n=140) were analyzed for Elemental Carbon (EC) and 1-NP. Urine samples (n=170) were analyzed for 1-NP metabolites using an HPLC-MS/MS assay. The association between 1-NP metabolites in urine and exposure to 1-NP in air was assessed using a regression model to determine if 1-NP urinary metabolites are a suitable biomarker for DE. Additionally, the suitability of survey data as a surrogate estimate for DE exposure was evaluated using a predictive model for 1-NP metabolites based on job and time-activity covariates. A range of EC and 1-NP exposures was observed (EC: GM=8.3µg/m3, GSD=2.5µg/m3; 1-NP: GM=35pg/m3, GSD=5.1pg/m3). A range of metabolite levels, consistent with the variability in exposure, was also observed (8-OHNP: 0.05-0.44pg/mL; 6-OHNP: 0.06-1.13pg/mL). Very few workers reported off-shift exposure to DE, suggesting that metabolite levels reflect occupational exposures. Levels of EC, 1-NP, and urinary metabolites in this cohort were high relative to environmental exposures, but were within the range of reported occupational levels.

Development of an LC-MS/MS Method for the Detection of Halogenated Furanones in Drinking Water

Laura Rascón Padilla
Occupational and Environmental Exposure Science, MS
Preceptor: Gretchen Onstad

Halofuranones are chlorine disinfection by-products (DBPs) that have been shown to be direct acting mutagens and are considered potential human carcinogens. These high priority DBPs are among the by-products to be analyzed for the USEPA's Integrated Disinfection By-product Research Project (Four Lab Study) developed to evaluate the toxicity of the complex mixture of DBPs present in treated water. The traditional method for characterization of halogenated furanones involves liquid-liquid extraction (LLE) and a time intensive derivatization step for gas chromatography analysis. In order to remove the derivatization step and provide a more efficient method to detect halofuranones in the Four Lab Study's water samples, we coupled a tandem solid phase extraction (SPE) sample preparation step with high performance liquid chromatography (LC) for subsequent mass spectrometry detection (MS/MS). Spiked deionized water samples were processed through tC18 and Osasis (HLB) SPE columns set in train, followed by analyte separation through reverse phase HPLC. A mobile phase linear gradient of 28-45% acetonitrile resulted in optimal peak shape and resolution within 20 minutes. Through UV detection with a diode array detector (DAD), tandem SPE coupled with HPLC yielded recoveries between 76-101% for halofuranones MX, BMX-1, BMX-2, BMX-3, MBA, and MCA, with relative standard deviations of less than 5%. Multiple reaction monitoring Parent-Product ion transitions were detected and optimized for all analytes with direct injection positive electrospray ionization (ESI) MS/MS using Agilent MassHunter Workstation Optimizer Software (version B.06.00). These preliminary results show that halofuranones can be ionized and detected through ESI MS/MS, and that the successful coupling of tandem SPE with HPLC may be paired with ESI MS/MS to generate a more efficient LC-MS/MS method for the characterization of halofuranones.

Evaluation of employment-related health impact assessments

Hee Yon Sohng
Occupational and Environmental Medicine, MPH
Preceptor: Bill Daniell

Aim: Health impact assessments (HIA) are tools that can be used to inform policy makers of the potential health consequences of their decisions. Reviews of HIAs related to housing and transportation have been performed, but little is known about employment-related HIAs. We identify the range of health issues addressed by employment-related HIAs, evaluate the process of conducting a labor-related HIA, and identify knowledge gaps for future HIA work.

Methods: A master list of completed HIAs was used to identify employment-related HIAs. These HIAs were coded for general descriptive statistics such as location, year of completion, depth, type of proposal, and health issues addressed. We also performed a process evaluation using guidelines adapted from existing practice standards.

Results: Reports from twenty-six prospective, employment-related HIAs conducted between 2004 and 2014 were available for review. Half of the HIAs were conducted in the United States, 23% were conducted in the United Kingdom, and 19% were conducted by the European Union (including one HIA from Ireland), 4% were conducted by practitioners in New Zealand and Palau, respectively. The majority (73%) of HIAs was performed in response to a proposed policy and 23% addressed a proposed project (23%). Over half of the HIAs examined how employment conditions such as flexible labor markets (European Union), paid sick leave (U.S.), and job security influenced health. Few HIAs assessed how physical/chemical/biological hazards influenced health.

Conclusion: HIAs were performed for a wide range of employment-related topics. In the US, HIAs are funded primarily through foundation support. Outside the US, governments typically funded HIAs which served more often as decision-support tool rather than an advocacy tool. This could result in greater engagement of decision makers in the HIA process in these countries. Review of the HIA process confirmed that while scoping, assessment, and reporting generally meet practice standards, more work is needed to improve plans to evaluate and monitor the more distal impacts of employment-related HIAs.

Characterization of Organophosphate Pesticides in Urine and Home Environment Dust

Catherine Tamaro
Environmental Toxicology, MS
Preceptor: Elaine Faustman

Farmers in Washington State use organophosphate pesticides to control harmful pests that might affect the quality of their products. Farmworkers, who perform thinning, harvesting, and other agricultural work, are often exposed to these pesticides and can carry home pesticide residues on their clothing, shoes, and skin, potentially exposing children in the household to pesticides. The University of Washington's Child Health Center (CHC) is interested in this occupational take-home pathway. Since 1999 the CHC has followed a community-based participatory research strategy in the Lower Yakima Valley to assess organophosphate pesticide (OP) exposure among farmworkers, their families, and non-farmworker families residing in the same communities.

This research characterizes the relationship between urinary OP metabolites vs. household dust OP residues by agricultural season, occupation, and adult/child status. The CHC study has collected household and vehicle dust, urine, blood, and saliva samples from farmworker and non-farmworker participants across the three agricultural seasons of the year. Seasonal urine, blood, and saliva samples were also collected from referent children between the ages of 2 and 6 who resided in the same participant households. Household dust samples were analyzed for the presence of OP residues while biological samples were analyzed for OP metabolites.

Dust samples from farmworker households had higher levels of the OP azinphos-methyl in each agricultural season than those from non-farmworker households. Farmworker households had higher levels of the urinary OP metabolite dimethyl thiophosphate (DMTP) than non-farmworker households. Household dust contained the highest levels of OP in the thinning season and the lowest levels in the non-spray season, regardless of household occupation. Farmworker households show evidence of higher levels of OPs in household dust and higher levels of urinary DMTP than do non-farmworker households.

Hand Massage as a Sponge Processing Method to Characterize Microbes in the Bullitt Center

Vivian Tran
Environmental Health, MS
Preceptor: Scott Meschke

Background: The Bullitt Center is a six-story, 50,000 square-foot green building that emphasizes energy efficiency and environmental performance based on design and operation. Microorganisms found in indoor surface environments most often come from human sources or by transport from the outdoor environment. Quantity and location of surface microbes can change due to re-aerosolization with human activity and building air movement. Few studies have been performed on surface microbes in green buildings. The goals are 1) to validate a sponge processing method based on literature reviews and 2) to characterize microbial populations from surfaces in the Bullitt building over a one-year period.

Methods: Three processing methods (shaker table, hand massage, and stomacher 400 circulator) were evaluated for microbial recovery from 3MTM sampling sponges with 10 ml neutralizing buffer. Sponges were spiked with 1.06E8 to 2.88E8 E. coli B cells and cells recovered by each method. DNA from recovered cells was extracted (MO BIO PowerSoilTM DNA Isolation Kit), quantified by nanodrop (ND-3300) using picogreen, and E. coli specific targets amplified by qPCR (with fluorescent probe). The best processing method was determined by examining both percent recoveries of CFU and C(t) values. The Bullitt surface samples were processed by the most efficient elution method followed by DNA extraction, nanodrop quantification of nucleic acid, and Illumina 16S metagenomic sequencing to characterize the microbes that were present.

Results: Hand massage was determined to be the most effective elution method based on the highest and most consistent calculated percent recoveries of CFUs ranging on average from 51.5-56.2%. C(t) values gave inconsistent results using undiluted nucleic acid, but tighter results using 10-fold dilutions of the sponge extractions ranging from (14.7-18.4% for shaker table, 12.5%-36.6% for hand massage, and 20.8-28.3% for stomacher) suggesting the presence of inhibitors. Throughout the study, nucleic acid results ranged from (0-5121.5 ng/ml). The highest nucleic acid values were observed in June ranging from (78.1-5121.5 ng/ml). Results from Illumina 16S (>10% OTUs) showed changes in microbial populations over time and by location.

Conclusion: Validation of hand massage as a sponge processing method was the best compared to the shaker table and stomacher methods and can be used for future studies to characterize microbial populations. Nanodrop and Illumina 16S results provided information in the change of quantity and location of surface microbes in the indoor environment. Such knowledge may help facilitate an understanding of the indoor microbiome and ultimately reduce human exposure to bacteria that cause adverse health effects.

Impact of Environmental Factors on Mosquito Populations and Distribution in King County, WA

Julia Weicheld
Environmental Health, MS
Preceptor: Charles Treser

Climate, land cover, and other environmental factors have been shown to have a direct impact on the epidemiology of vector-borne diseases. Warming temperatures combined with other effects of climate change and changes in land use have the potential to amplify vector mosquito populations and transmission of arboviruses such as West Nile Virus (WNV) in Washington. The relationship of vector-borne disease transmission with the environment is complex and highly localized. To date, very little research has been conducted on this issue in Washington State. This research aims to provide insight into vector populations that may govern vector-borne disease transmission in King County, WA. Mosquitoes were trapped at selected areas in King County during the summer of 2014. Additional mosquito data collected by previous DEOHS students and the WA State Department of Health were gathered and assessed for quality and completeness. Four identical sites sampled in 2003 and 2014 were directly compared to assess any changes in mosquito abundance and diversity over an 11-year period. Temperature, precipitation, and land cover data were obtained and investigated for their influence on mosquito abundance during these seasons. Our results indicate that mosquito abundance was significantly higher in 2003 than in 2014. Culex pipiens was the dominant species both years, although in 2014 there appeared to be greater mosquito diversity. Medium-high developed land cover was significantly associated with Culex pipiens abundance. Total mosquito abundance was associated with maximum temperature, with higher temperature weeks having greater numbers of mosquitoes. The relationship of mosquito abundance with precipitation remains less clear. These results suggest that mosquito abundance is related to environmental factors in King County, however more research should be done to better understand these and other influences on mosquito populations.

Developing Tools for evaluating and enhancing clinician outreach training on pesticides and child health

Margaret Willis
Environmental and Occupational Health, MPH
Preceptor: Butch de Castro

A survey of healthcare providers and community health workers serving agricultural areas in the Pacific Northwest found that only 22% report any training on pesticides and child health and 61% report feeling uncomfortable responding to questions from patients on the topic. In response, the Northwest Pediatric Environmental Health Specialty Unit (NW PEHSU) developed a 1-hour in person outreach training course for clinicians. The goal of this practicum project was to develop tools to evaluate and enhance efforts by the NW PEHSU to increase clinician knowledge and confidence on the topic. First, an evaluation tool was created to measure: 1. level of knowledge through multiple-choice questions on important concepts in pesticide and child health; and, 2. level of confidence through survey questions modified from published peer review research on self efficacy. Effectiveness was defined as an increased score and/or confidence rating in post-training testing compared to pre-training testing. On average, training participants showed both increases in test scores and self-efficacy ratings. The results support the effectiveness of NW PEHSU's outreach trainings. Second, a factsheet was created that summarized key information from the outreach training on recognizing exposures, proper management, and providing guidance for prevention. An online survey was generated to get feedback on its content, design, and perceived usefulness. It was administered to volunteers from outreach trainings and clinicians identified by the NW PEHSU director. Respondents who had attended training agreed with statements that the factsheet reinforced key information and added value to the training. Next steps should include: incorporating survey feedback into the final version of the factsheet and placing it online; measuring use of the factsheet by how often the page is visited online or how often the file is downloaded; and, retesting clinicians who attended training for retention of knowledge and sustained level of reported self-efficacy.

Exploring clinician training on pesticides and child health and developing curriculum aimed at enhancing self-efficacy

Margaret Willis
Environmental and Occupational Health, MPH
Preceptor: Catherine Karr

Research shows that few clinicians receive training on pesticides and child health. Clinicians report low levels of confidence, or self-efficacy, in addressing pesticides compared to other environmental exposures. In 2006, the Northwest Pediatric Environmental Health Specialty Unit and the Pacific Northwest Agricultural Safety and Health Center published an online education module for clinicians on organophosphate pesticides and child health, to address this gap. Since its publication, new evidence is available on the health effects of organophosphate pesticides, and on changes in patterns of pesticide use that make exposure to pyrethroid and other pesticide classes more common. The objectives of this project were to: revise the 2006 module to reflect the latest scientific evidence on organophosphates; expand the content to include carbamate and pyrethroid pesticide classes; and, develop a tool to measure its effectiveness at increasing clinician knowledge and ratings of self-efficacy. First, a need for the project was evaluated through an informal survey of clinicians attending in person trainings on pesticides and child health. The survey supported the need, with over 50% of participants reporting no previous training and 82% stating they would be interested in completing an online module for continuing education credit on the topic. A literature review was done using PubMed to update existing content and develop new content on carbamate and pyrethroid exposures. An expert reviewed the content and revisions were made. A pre and posttest were created to evaluate the effectiveness of the online module in increasing clinician knowledge and ratings of self-efficacy. Next steps should include: programming the content into an online module; testing the module on a small group of clinicians and making adjustments based on feedback; obtaining certification for continuing education credits and making the module available at no charge online; and, continued evaluation of effectiveness through pre and post testing.

BEBTEH stands for Biostatistics, Epidemiologic and Bioinformatics Training in Environmental Health

The following abstracts are from PhD students whose research are funded by this training grant. The National Institute of Environmental Health Sciences federal training grant (ES015459) supports predoctoral and postdoctoral trainees from the Departments of Biostatistics, Environmental and Occupational Health Sciences, Epidemiology, and Genome Sciences who are pursuing quantitative training with environmental health science applications.

Quantitative Microbial Risk Assessment of salmonellosis for owners of backyard poultry flocks, Seattle, WA

Heather Fowler
Environmental and Occupational Health, PhD
Preceptor: Peter Rabinowitz

Background: The practice of urban chicken farming has been gaining popularity in major US cities nationwide and in some other countries. Urban farmers may be unaware of the zoonotic risks associated with animal rearing. Zoonotic diseases from poultry include influenza, campylobacteriosis, and salmonellosis. Over the past 20 years, more than 45 outbreaks in the US have been linked to baby poultry purchased to supply backyard flocks. Quantitative microbial risk assessment (QMRA) is a method to explicitly calculate exposure risk. We conducted a QMRA of salmonellosis from backyard flocks.

Methods: From June 1-Oct 1 2014 we performed a convenience sample of backyard flocks in the Seattle Metropolitan area. Flock owners were video recorded while providing routine care to their birds and video notational analysis performed to estimate the rate of contamination and possible self-inoculation. Hand swabs were collected before and after routine care to estimate Salmonella transfer. A series of environmental swabs were collected from the interior of the coop to estimate environmental Salmonella contamination. A 62-item survey was also completed by flock owners reviewing animal inventory and husbandry practices, as well knowledge, attitude and practices of the flock owners related to Salmonella. Using CrystalBall® software and exposure frequencies identified in the study a quantitative microbial risk assessment was performed modeling scenarios of high and low environmental contamination.

Results: A total of 50 residents participated in the study. Flock owners on average owned 5 hens, with a range of 2-18 hens. On average poultry caretakers touched potentially contaminated poultry surfaces including the interior of the coop, bird feed and feeding equipment, eggs, and chickens 13.0 +/- 5.2 times while conducting their poultry care routine. Potential sources of self-inoculation involved touching the face, touching the mouth directly and placing fingers in the mouth as well as kissing chickens and was observed on average 1.2 +/- 1.6 times during poultry care routines. Cross-contamination which serves as a means to expose those not directly in contact with poultry environments was measured by the number of times flock owners wiped their hands on their clothing, held birds close to their person and wore flock shoes in the house. These situations were noted 1.9 +/ 1.9 times per routine.

Conclusions: Our modeled risk of Salmonella exposure in backyard poultry suggests value in preventive measures. Such measures include personal protective equipment and hand hygiene.

Estimating Average Ambient Air Pollution Exposure across Zip Codes: A Simulation Study

Karen Hinckley Stukovsky
Epidemiology, PhD
Preceptor: Lianne Sheppard & Joel Kaufman

Background: In many studies, individual-level health effects are of interest, but exposure is not measured at the individual level, or exposure location(s) is not known. In other studies, effects of interest are at the area-level, such as zip code or county. Known locations, such as U.S. Census Bureau-defined geolocations, are easily accessible and are beneficial in studies of the association between ambient air pollution and health outcomes. The purpose of this pilot study was to evaluate how many locations are needed, within a zip code, to estimate ambient air pollution exposure across census-defined zip code tabulation areas (ZCTAs).

Methods: 50 zip codes, limited to the 48 contiguous U.S. states, were randomly selected from the United States Cystic Fibrosis Foundation Patient Registry (CFFPR) and matched to the 5-digit U.S. Census 2000 ZCTA. 20 census blocks, located in each of the 50 ZCTAs, were selected via population-weighted random sampling. Ambient air pollutant concentrations for PM2.5 were calculated at each of the selected census block centroids using the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air) National PM2.5 and National NO2 models for Year 2000. Using these estimates, a Monte Carlo bootstrap was used to construct 1,000 samples each for 1 to 20 locations within each ZCTA to evaluate the number of locations needed to minimize the coefficient of variance (CV) for mean PM2.5 or NO2 averaged at the zip code level.

Results: 27 contiguous U.S. states were represented in the 50 selected zip codes. Six (12%) of selected zip codes were in California. The mean number of housing units in the zip codes was 11,562.6 units (SD: 5,973.3; Range: 1,132 – 24,770). Average size of the zip code land area was 217,293,835 m2 (SD: 280,550,886 m2). Overall mean PM2.5 was 13.28 μg/m3 (SD: 2.84 μg/m3). Mean ZCTA-level PM2.5 ranged from 6.12 – 20.08 μg/m3. Overall mean NO2 was 13.54 ppb (SD: 5.89 ppb). ZCTA-level mean NO2 ranged from 1.78 – 11.6ppb. Overall CV, for PM2.5, ranged from 23.26, with two locations, to 21.36 with 20 locations and 44.87 to 43.50 for NO2.

Conclusions: Overall, averaging a higher number of census block locations improved the variance in the mean estimates for PM2.5 and NO2 at the ZCTA-level, though, the differences in CV leveled off above 10 locations for PM2.5 and NO2. Future work includes looking at the effect of ZCTA land mass and housing volumes on the number of locations to be averaged.

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Instrumental Variables for Survival Models with Endogenous Regressors

Jun Hwang
Biostatistics, PhD
Preceptors: Gary Chan & Lianne Sheppard

In linear and generalized linear regression settings, bias from the lack of adjustment for unobserved confounders has been studied extensively. Adjustment using instrumental variables is one approach to this estimation problem that has been used widely in economics. In the typical language of regression, omission of unobserved confounders results in error terms that are correlated with the covariate of interest. An instrumental variable is a covariate that is associated with the exposure of interest, affects the outcome of interest only indirectly through the exposure of interest, and cannot be plausibly associated with any unobserved confounders. Under a few additional assumptions, instrumental variables can be used to provide consistent estimates for the effect of the exposure of interest. Many outcomes of interest in medical research settings are concerned with the amount of time until a certain, well-defined event. Often, this event is death, and such research is typically referred to as survival analysis. Until relatively recently, survival analysis models have not been able to provide consistent estimates in the absence of confounders. We examine the implementation of instrumental variables methods under an additive hazards framework. We then apply this model to estimate the effect of endotoxin exposure on survival outcomes for textile factory workers in Shanghai.

Covariate-adaptive Clustering of Exposures for Air Pollution Epidemiology Cohorts

Joshua Keller
Biostatistics, PhD
Preceptors: Adam Szpiro

We present a novel clustering approach for analyzing multivariate environmental exposures and health outcomes in cohort data. This is motivated by work in air pollution epidemiology, where multi-pollutant exposure data are available from regulatory monitoring networks. Dimension reduction methods can simplify analyses of multivariate exposures, but the misalignment of monitor and cohort locations requires a way to predict reduced-dimension exposure where no monitoring data exist. We present a method that uses geographic covariate information to cluster multi-pollutant observations and predict cluster membership at cohort locations. Our predictive k-means procedure can be derived as a mixture of normal distributions incorporating multinomial logistic regression and is fitted using a version of the EM algorithm. We compare this approach to k-means clustering followed by spatial prediction. In simulations, we demonstrate that predictive k-means can reduce prediction error by over 50% compared to k-means, with minimal loss in cluster representativeness. In a re-analysis of the NIEHS Sister Study cohort using predictive k-means, we find that the association between systolic blood pressure (SBP) and long-term fine particulate matter (PM2.5) exposure varies significantly between different clusters of PM2.5 component profiles. Our cluster-based analysis shows that for subjects assigned to a cluster located in the Northern U.S., a 10 ug/m3 difference in PM2.5 is associated with 4.70 mmHg (95% CI, 2.13, 7.27) higher SBP.

Black carbon and ultrafine particle counts downwind of two major airports

Erin Riley
Environmental and Occupational Health, Postdoctoral Student
Preceptor: Christopher Simpson

Recent measurements of ultrafine particle (UFP) number counts up to 10 kilometers downwind of airports have revealed the presence of an elevated UFP impact that closely resembles the landing routes of aircraft. Using a mobile platform, we have investigated the relationship between simultaneous UFP number counts at different lower size thresholds, UFP count mean diameter and black carbon mass at locations under the aircraft descent path of the Los Angeles international airport (LAX) and Hartsfield–Jackson Atlanta International Airport; these airports are the third and first busiest airports in the world. Preliminary findings at LAX suggest that the excess UFP observed are predominately black carbon particles in the range of 25 to 35 nm. The black carbon concentrations predicted by traditional dispersion models for aircraft using emission factors for engine loads typical of landing are underestimated compared to those measured. The model is improved by including additional downward transport of engine exhaust as a result of large scale vortices induced by the aircraft. These findings further support the need to reassess the impacts of air traffic on air quality in neighborhoods surrounding airports.

Heterogeneity in Quantum Dot Induced Lung Inflammation and Toxicity in Recombinant Inbred Mouse Strains from the Collaborative Cross

David Scoville
Environmental Toxicology, PhD
Preceptor: Terrance Kavanagh

Quantum dots (QDs) are engineered nanoparticles commonly composed of a CdSe/ZnS core/shell and outer coatings specific to their potential use in electronics, research, and medicine. However, their small size and heavy metal composition has generated concerns regarding their toxicity. Nanoparticle toxicity is composition and coating dependent, and it would be impractical to do comprehensive mechanistic studies on all nanoparticle formulations. Thus we propose that systems genetics could be useful for efficiently identifying genes and pathways associated with nanoparticle toxicity, and prioritizing them for further mechanistic interrogation. The Collaborative Cross (CC) has been shown in recent studies to be an excellent resource for carrying out such systems genetics-based studies.

In prior work, we found that the 8 inbred founder strains of the CC varied widely in their susceptibility to QD-induced lung inflammation and toxicity. Since the RI strains are unique combinations of the founder genomes and because of the polygenic nature of the inflammatory response, we hypothesized that the RI strains would also vary in their susceptibility, and that we might observe phenotypes that were outside the range of those present in the 8 founder strains.

We observed significant heterogeneity among 12 RI strains of the CC in biomarkers of QD-induced lung inflammation 8 h after oropharyngeal aspiration. These included the percentage of neutrophils, the levels of total protein, and levels of lactate dehydrogenase (LDH) in bronchoalveolar lavage fluid (BALF). Lung tissue heme oxygenase (HMOX1) levels also varied by strain and were weakly but significantly correlated with lung tissue glutathione (GSH) levels. Also, BALF LDH was weakly correlated with total protein levels and this relationship was stronger in QD treated mice than saline treated mice. For some of the RI strains, BALF protein levels and percent neutrophils were outside the range of the founder strains. Interestingly, lung tissue GSH levels varied less among the RI strains, than among the 8 CC founder strains.

Our findings support future systems genetics studies using genotype, phenotype, and gene expression data, in which we will hopefully identify candidate susceptibility genes. Measuring the transcriptome of the RI strains using RNA-Seq is currently in progress. This study will provide insights into mechanisms of QD related toxicity, help to identify biomarkers of susceptibility, and ultimately provide information for the design of safer engineered nanomaterials. Supported by NIEHS grants U19ES019545, P30ES007033, T32ES007032, and T32ES015459.

The Population Oral Microbiome of Individuals Living in a Farming Community Reveals an Agricultural Oral Microbiome Signal

Ian Stanaway
Environmental Toxicology, PhD
Preceptor: Elaine Faustman

Characterizing the population census bacterial diversity of the microbiome has just begun. Efforts such as the Human Microbiome Project piloted a selection of urban individuals to identify the core microbiome shared by many people. Our diverse environment including, rural agricultural contexts, provide niche exposures to many animals and plants with colonizing bacteria not common in other environments. At the University of Washington's Center for Child Environmental Health Risks Research we are characterizing agricultural exposures to a community cohort of predominantly Hispanic farmworkers and their children within the Yakima Valley farming region of Eastern Washington. In a subset of the cohort, we analyzed the oral microbiomes of 121 adults by collecting 206 oral buccal samples across two seasons (Summer 2005 and Winter 2006) and DNA sequenced of the V5 and V6 regions of the bacterial 16S ribosomal RNA gene. Using the bacterial sequence data we ascertained the oral bacterial taxonomic diversity of these individuals' oral microbiomes.

By comparing to bacteria detected in the oral cavity by three other available urban oral microbiome projects' sequence data (The Human Microbiome Project, the Human Oral Microbiome Database and a report of urban Chinese students' microbiomes), there is large overlap with 119 of 263 the bacterial genera detected in common. Bacterial genera with large differences in prevalence between the Yakima Valley cohort and other cohorts were reviewed in the literature. We find the literature supports these as bacteria representative of an Agricultural Oral Microbiome signal and distinct from bacteria detected in urban oral microbiomes. This signal of prevalent agriculturally derived bacteria in the Yakima population is consistent with the agricultural influence of exposure to animals with potential respiratory disease, soil and plants. Specifically the genera Mannheimia, Nicoletella, Parachlamydia, Suttonella, Actinobacillus, Alicyclobacillus and Pantoea are identified as resulting from agricultural sources based upon their respective animal and plant host natures. Hispanic dietary influences on the oral microbiome were also evident by the detection of Enhydrobacter and Xylanibacter due to their respective detection by others in Mexican Artisanal Poro cheese and rural agricultural populations that consume high fiber unprocessed foods. Additionally we also detect Phocoenobacter which previously had only been identified in dolphins, Amazonian Amerindians and rural Africans. Thus bacterial census analysis of individuals' oral microbiomes from an agricultural environmental context identifies bacteria not previously identified as common to the oral niche.

Using Phylogenetics to Better Understand the Epidemiology of Escherichia coli O157: Methods and Conceptual Framework

Gillian Tarr
Epidemiology, PhD
Preceptor: Jonathan Mayer

Background: Escherichia coli O157:H7 is an important foodborne illness in the United States, estimated to cause over 60,000 cases and 2,000 hospitalizations each year. It is one of the highly pathogenic Shiga toxin-producing forms of E. coli (STEC) and is the most common cause of hemolytic uremic syndrome (HUS), which can result in kidney failure and death. Individual strains within the STEC O157 serotype can vary substantially in their virulence, and genetic characteristics of the bacterium may be responsible for a large portion of this variation. Previous studies have suggested that STEC O157's phylogenetic tree can be used to explain some of the variation in severe clinical outcomes. However, these studies have relied on phylogenetic classifications based on limited genetic information. The methods used to analyze the association have also not fully accounted for some critical features of the data, such as strain-specific incidence rates and the role of specific Shiga toxin subtypes.

Approach: The current study attempts to remedy these deficiencies. An expanded phylogenetic tree will provide the basis for analyzing the association between lineage and clinical outcomes, including HUS. Rigorous epidemiologic methods will be employed to more fully test the association as compared to past studies. Additionally, this study will examine characteristics of the communities where cases live that may influence the distribution of disease, both overall and by lineage. To consider how best to approach the study questions, a conceptual framework was developed encompassing factors in STEC O157 disease occurrence at the pathogen, individual host, and community levels.

Methods: The Washington State Department of Health (DOH) provided isolates from all 1,372 culture-confirmed STEC O157 cases reported 2004 to 2014. To determine which cases to type for phylogenetic lineage, a stratified sampling scheme was developed to ensure adequate representation of all STEC O157 strains observed during the study period. Selected strains are being analyzed to define phylogenetic lineage. They will then be combined with clinical data to test the association between lineage and clinical outcomes. Mediation by specific subtypes of Shiga toxin genes will also be formally tested. Finally, cluster detection techniques and multilevel models will be used to explore the distribution of STEC O157 in Washington State and potential drivers of infection. This study demonstrates the potential for combining phylogenetic and epidemiologic methods to enhance our understanding of STEC O157 epidemiology.

Inference following adaptively designed group sequential studies

David Whitney
Biostatistics, PhD
Preceptor: Scott Emerson & Lianne Sheppard

Group sequential study designs (GSDs) have been proposed in the clinical trial literature to allow early study termination for treatment futility or efficacy. GSDs are more ethical than a fixed sample study because they prevent participants from taking ineffective or potentially harmful treatments and allow the beneficial treatments to be approved sooner for the general population. A GSD is defined by a set of stopping rules at a series of pre-specified interim analyses. More generally, adaptive group sequential studies (AGSDs) allow for arbitrary unplanned modifications to future analysis times and stopping rules based on results from an interim analysis. To maintain the nominal Type 1 error rate for an AGSD, Brannath, Mehta and Posch (2009) and Gao, Liu and Mehta (2013) propose projecting the observed outcome from an adaptive design onto a reference group sequential design. Their projections are constructed to maintain analysis time-based conditional error (ATCE). We modify the ATCE procedure by using the conditional error rate with respect to the likelihood ratio (LRCE) to project the observed outcome onto the reference design. In a variety of simulation settings, we find that using LRCE projections instead of ATCE projections results in a lower mean-squared error and narrower confidence intervals for the median unbiased estimate of treatment effect in AGSDs.

Assessing Indoor Radon Exposure on the Navajo Nation

Sheldwin Yazzie
Occupational and Environmental Hygiene, PhD
Preceptor: Michael Yost

The purpose of this dissertation research project is to assess indoor radon exposure in homes on the Navajo Nation. This area sits on the Colorado Plateau, a region naturally enriched with high levels of uranium. Radon is a gas that has no color or odor, and it is a product of natural uranium decay. Radon is a known human lung carcinogen, and is able to pass from the soil into homes.

According to the American Cancer Society and the US Environmental Protection Agency (EPA), radon is the second leading cause of lung cancer in the USA behind smoking. Health effects from radon exposure have been well established in studies of uranium miners in the Southwest. However, fewer studies have examined health effects from low-level indoor radon exposure in residential settings. The average indoor radon levels as measured in US homes is 1.3 pCi/L. The EPA states that indoor levels should not be greater than 4 pCi/L, but really there are no safe levels of radon exposure. Reducing radon levels in homes with high exposures is an important intervention that can help prevent non-occupational lung cancer.

Radon is found in the soil, rocks, and water in this area of the Southwest and throughout other parts of the US. Radon may enter homes in a few ways. One entry pathway is through cracks in the floors or walls. A second pathway is directly from contaminated uranium waste materials, which may have been used to build some homes. A third source of radon is the gas dissolved in groundwater. Radon levels often are higher in the winter when windows and doors are closed.

This proposed dissertation research project has three primary goals. One goal of this project is to be able to predict radon exposure levels inside homes on the Navajo Nation. Researchers in Switzerland were able to estimate indoor radon exposures using a prediction model. If we can develop a similar type of prediction model for this area, it could be very useful in identifying homes with potentially high levels of indoor radon. By finding homes with potentially high levels of indoor radon, then we can help homeowners find ways to reduce their radon exposure. A second goal of this project is to collect indoor radon measurements from a group of volunteers from the Community Uranium Exposure Journey To Healing Program (CUEJTH) that is based in Shiprock, NM. The mission of the CUEJTH program is to provide health monitoring, health promotion and health education to communities who have been exposed to uranium across the Navajo Nation. Collecting these measurements will help us to determine if the model makes accurate predictions of indoor radon levels, which is a third goal of this project.