TITLE: Intersection between exposures to environmental contaminants, immune function, and infectious diseases

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STUDENT SUBMISSION: Yes

TOPIC/TARGET AUDIENCE: Researchers, policy makers, and community outreach personnel

ABSTRACT: Infectious disease remains one of the leading causes of morbidity and mortality. This panel will explore the growing evidence that exposure to naturally occurring and anthropogenic environmental contaminants can influence the developing immune system, vaccine antibody levels, infectious disease risk, and antimicrobial resistance in bacteria. Specifically, we will focus on the association between metals and PAHs on these immunological outcomes and susceptibility to infectious diseases. Our panel showcases three projects exploring this environment contaminant using population-based studies conducted in the United States and Bangladesh. Namely, we will present data collected in the US National Health and Nutrition Examination Survey that identified associations between arsenic and PAHs and hepatitis B serology. Next, we will present data from a prospective birth cohort conducted in Bangladesh that examined the association between metal exposures during critical immune developmental stages and vaccine antibody levels and infectious disease incidence in young children. Finally, we will present the results from a systematic literature review examining the association between metal exposures and antibiotic resistant bacteria in the environment.

OBJECTIVE(S): 1. Describe how environmental contaminants can influence immune functioning that could influence susceptibility to infectious disease.

2. Explain associations between exposure to environmental contaminants (arsenic and polycyclic aromatic hydrocarbons) and infectious disease outcomes including humoral immunity and symptomatic disease.

3. Compare the strengths and limitations of different epidemiological study designs for examining the relationship between environmental pollutants and infectious diseases.

PANEL MODERATOR: Molly L. Kile

PANEL ABSTRACT 1: Background: Approximately 850,000 Americans currently live with acute or chronic Hepatitis B infection. Exposure to polycyclic aromatic hydrocarbons (PAHs) and arsenic are known to impact the immune system and may influence susceptibility to hepatitis B.

Methods: We used multiple cycles of the National Health and Nutrition Examination Survey to evaluate the cross-sectional associations between urinary PAH metabolites, arsenic, and serological markers of hepatitis B. Logistic regression models estimated the association between urinary biomarkers and 1) natural hepatitis B infection, 2) protective vaccination serology.

Conclusions: People with the highest exposure to 1-pyrene had over twice the odds of natural infection (ORadjusted: 2.04 for highest-to-lowest tertile, 95% CI: 1.31, 3.16). Additionally, there was a positive association between arsenic exposure and odds of natural infection (ORadjusted: 1.40 per ln unit, 95% CI: 1.15, 1.69). People within the highest tertile of 1-napthol, 2-napthol, 3-fluorene, 2-fluorene, 1-phenathrene, 1-pyrene, or total PAHs had lower odds of serology indicative of protective hepatitis B vaccination serology. These results suggest that arsenic exposure may increase susceptibility to natural infection whereas PAH exposures may decrease the odds of a protective hepatitis B vaccine response.

PRESENTER 1: Faye V. Andrews

PANEL ABSTRACT 2: Background: Exposure to arsenic during early life may modulate humoral immunity. This study examined the association between arsenic exposure and vaccine-antibody concentrations measured in early childhood. Methods: A prospective birth cohort was recruited in Bangladesh (2008-2011). Drinking water arsenic was measured at enrollment ($\leq$16 weeks gestation), age 20-40 months, and at age 5. Serum was collected at age 5 (N=502). Concentrations of diphtheria and tetanus toxoid IgG were quantified. Antibody concentrations above 0.1 IU/mL were considered sufficient for clinical protection. Multivariate regression models assessed the associations between arsenic and vaccine antibodies.. Conclusions: Diphtheria IgG was associated with in utero arsenic exposure. A doubling in maternal drinking water arsenic during pregnancy was associated with a 6.1% decrease in anti-diphtheria concentrations at age 5 (95%CI: -12.2%, -0.01%) adjusting for subsequent arsenic exposures and confounders. Children within the highest-versus-lowest tertile of in utero arsenic exposure had a greater odds of falling below clinically sufficient diphtheria titers (ORadjusted:1.89, 95%CI: 1.02,3.49). Stratified results showed inverse associations between both diphtheria and tetanus to in-utero arsenic exposure among children classified as female, stunted growth, or underweight.

PRESENTER 2: Molly L. Kile

PANEL ABSTRACT 3: Background: Previous research showed that high levels of in utero arsenic exposure increased the risk of infectious disease in the first year of life. It is unclear if this association persists throughout childhood.

Methods: A prospective birth cohort study examined the association between arsenic exposures and respiratory, diarrheal, and febrile morbidity in Bangladeshi children age 4-5 years (n=989). Household drinking water samples were used to estimate arsenic exposure in pregnancy, toddlerhood, and childhood. Children were actively surveyed for symptoms every 2 weeks from age 4-5 years. Poisson regression estimated the association between arsenic exposure at each developmental stage and respiratory and febrile illness adjusting for confounders.

Conclusions: We observed 103 respiratory, 1 diarrheal, and 78 febrile illnesses, limiting further analysis of diarrhea. The incident rate ratios (IRR) for each unit increase in natural log drinking water arsenic during pregnancy was IRR=1.1 (95% CI: 1.0, 1.3) and IRR=0.8 (95% CI: 0.7, 1.0) for respiratory and febrile illness, respectively. Drinking water arsenic exposure in pregnancy

(but not toddlerhood and childhood) may be influencing infectious disease risk in children aged 4-5 years in Bangladesh. However, the increased risk appears to be modest.

PRESENTER 3: Sharia M. Ahmed