Exposure to Volatile Organic Compounds in Drinking Water and Specific Birth Defects and Childhood Cancers at U.S. Marine Corps Base Camp Lejeune, North Carolina

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1998 ATSDR Study on Adverse Pregnancy Outcomes

• Evaluated potential maternal exposure to drinking water contaminants on base and
  – Preterm birth
  – Small for gestational age (SGA)
  – Mean birth weight deficit

• Only used available databases
  – Electronic birth certificates beginning in 1968
  – 12,493 singleton live births on base during 1968-1985
  – Base family housing records linked to mother’s address at delivery and father’s name in most cases
  – Could not evaluate birth defects and childhood cancers
1998 ATSDR Study on Adverse Pregnancy Outcomes: Results

• Exposure to TT water (PCE)
  – Elevated risk for SGA among infants born to
    – Mothers aged >35 years
    – Mothers with ≥2 prior fetal losses

• Exposure to HP water (TCE)
  – Elevated risk for SGA only among male infants

• Recently discovered exposure misclassification requires reanalysis of study data
Current ATSDR Case-Control Study

• Exposure to VOCs in Drinking Water and Specific Birth Defects and Childhood Cancers

• Multi-step process
  – Review scientific literature to identify specific birth defects and childhood cancers associated with drinking water contaminated with chlorinated solvents
  – Conduct telephone survey to ascertain potential cases
  – Obtain medical records to verify diagnoses of reported cases
  – Conduct a case-control study
Current ATSDR Case-Control Study

• The following outcomes were selected for further study based on the scientific literature

  – Neural tube defects (NTD)
  – Oral cleft defects (cleft lip and cleft palate)
  – Conotruncal heart defects
    – tetralogy of Fallot
    – D-transposition of the great arteries
    – truncus arteriosus
    – pulmonary valve atresia with ventricular septal defect
    – double outlet right ventricle
  – Choanal atresia (a nasal defect)
  – Childhood leukemia
  – Childhood non-Hodgkin’s lymphoma
Current ATSDR Case-Control Study

• Telephone survey conducted to identify potential cases of the selected adverse childhood outcomes among births occurring during 1968-1985 to mothers residing on base any time during their pregnancy
  – 16,000-17,000 estimated births

• Parents of 12,598 eligible children were surveyed
  – Overall participation rate of 74%-80%
Current ATSDR Case-Control Study

- Sufficient numbers of NTDs, oral clefts, and childhood cancers reported
  - 106 reported cases
    - 35 NTDs
    - 42 oral cleft defects
    - 29 childhood hematopoietic cancers

- Verification of diagnoses of cases ascertained by survey has been completed
Current ATSDR Case-Control Study

• 52 confirmed cases (51 parents interviewed)
  – 15 NTDs
  – 24 clefts
  – 13 hematopoietic cancers
• 32 confirmed not to have the reported diseases
• 8 refused to participate
• 7 could not be verified (no medical records)
• 7 were ineligible
Current ATSDR Case-Control Study

- Parents of 548 controls were interviewed

- Parental interviews conducted in 2005 to obtain information on
  - Maternal water consumption habits
  - Maternal residential history
  - Maternal exposures during pregnancy
  - Parental risk factors

- Review of base family housing records to verify dates and location of mother’s reported residence on base
Data Analysis

• Separate analyses will be conducted
  – NTDs
  – Oral clefts
    – cleft lip (with or without cleft palate
    – cleft palate
  – Childhood leukemia/NHL
Data Analysis

- Analyses will evaluate both continuous and categorical drinking water contaminant variables
  - Smoothing methods will be used to suggest categorical variable cutpoints
  - Each contaminant will be analyzed separately
  - Joint effects of contaminants will also be evaluated
Confirmed cases of NTDs

- Average and maximum contaminant level over the first trimester
- Average and maximum contaminant level during the period 3 months prior to date of conception (DOC)
- Average level in the first month of pregnancy
Data Analysis

Confirmed cases of oral cleft/oral palate defects

• Average and maximum contaminant level over the first trimester
• Average and maximum contaminant level during the period 3 months prior to DOC
• Average level in the second month of pregnancy
Data Analysis

Confirmed cases of childhood cancers (leukemia and non-Hodgkin’s lymphoma)

- Average and maximum contaminant level over each trimester
- Average and maximum contaminant level over the first year of child’s life
- Average and maximum contaminant level during the period 3 months prior to DOC
- Cumulative exposure over the pregnancy and first year of child’s life
PCE Contamination Levels (ppb) from Tarawa Terrace by Gestational Month: Example

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Data Analysis

• Compute unadjusted and adjusted results using logistic regression and calculate 90% confidence intervals
  – If data too sparse, conditional or exact logistical regression may be used

• Include in final model potential confounders that contribute to a ≥10% change in the parameter estimate for the exposure variable

• Evaluate categorical variables for water usage obtained from interviews, alone and in combination with the contaminant levels
Data Analysis

• Sensitivity analysis to assess the impact of exposure misclassification

• Consider secondary analyses including cases and controls with incomplete residential history or cases that could not be confirmed by medical records

• Interpretation of results based on
  – Magnitude of association
  – Exposure-response relationship
  – Biological plausibility
  – Consistency with other studies