Parental Pesticide Exposure and Measures of Thyroid Function in Their Offspring

Paul A Romitti, PhD

Professor, Department of Epidemiology, Department of Biostatistics, and the Interdisciplinary Program in Toxicology, University of Iowa

Director, Iowa Registry for Congenital and Inherited Disorders

Director, Iowa Center for Birth Defects Research and Prevention

Director, Reproductive Molecular Epidemiology Research and Education Program

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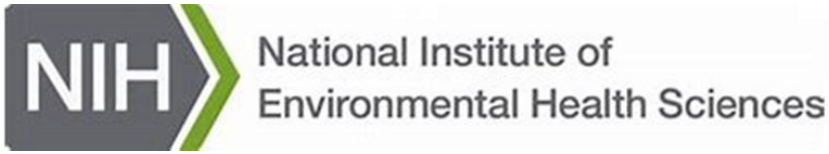
Collaborators

J Suhl, PhD
C Lynch, MD, PhD
J Oleson, PhD
K Conway, PhD
V Sheffield, MD, PhD
A Rhoads, MS
Liuska Pesce, MD
S Berberich, PhD

L Beane Freeman, PhD



D Sandler, PhD

BACKGROUND

Congenital Hypothyroidism (CH)

- Disorder defined by a deficiency in thyroid hormones and is one of the most common metabolic conditions present at birth
- Multiple forms of CH (central, primary, transient) have been identified; central and primary CH require lifelong treatment
- Primary CH affects about 4 per 10,000 children and often results from thyroid dysgenesis
- U.S. incidence of primary CH has increased about 3% per year since 1990, but factors contributing to this increase are unclear
- Iowa NBS Program tests for primary but not central CH with follow-up testing and diagnosis conducted by the University of Iowa Stead Family Children's Hospital

Etiology of Primary CH

- **Multifactorial (genetic, non-genetic), but not well understood**
- **Descriptive studies reported several factors associated with CH**
  - Infant sex and anthropometrics (female, low/high birthweight, preterm birth, plural pregnancy)
  - Maternal demographics (>39 years, non-Hispanic White)
- **Animal and human studies suggest associations between maternal pesticide exposure and CH in offspring, but studies are limited and equivocal**
- **No studies of paternal pesticide exposure and CH**
- **Findings from the Agricultural Health Study (AHS) suggest that pesticides may be associated with adult hypothyroidism**

Hypotheses

- Impaired newborn thyroid function, defined by newborn elevated TSH, is associated with parental occupational pesticide exposures during pregnancy

- Parental exposure to pesticides during pregnancy is positively associated with diagnosis of primary CH in offspring

Aims

- Link Iowa AHS participant offspring data with the multi-decade repository of Iowa NBS data

- Examine associations between parental pesticide exposure during pregnancy reported by AHS participants and thyroid function and diagnosis of primary CH among their offspring

Agricultural Health Study (AHS)

- Design: Prospective cohort study
- Cohort: Pesticide applicators and their spouses who reside in Iowa or North Carolina
- Enrollment: 1993 – 1997 at licensing facilities for use of restricted pesticides in each state
- Outcomes: Cancer and non-cancer outcomes among applicators and spouses

Data Collection – Enrollment

- Enrollment questionnaire
- Applicator questionnaire

- Spouse questionnaire
- Female and Family Health questionnaire

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Data Collection – Follow-Up

- **Active**

Phase I Questionnaires (1993-1997)

- Applicator & Spouse
  - General information
  - Farming operations
  - Pesticide use
  - Work practices
  - Non-farm work
  - Lifestyle behaviors
  - Physical activity
  - Dietary/cooking practices
  - Health history
  - Family history
  - Home information (spouse)
  - Reproductive health/ history (spouse)
  - Live born children (spouse)

Phase II Interviews (1999-2003)

- Applicator & Spouse
  - General information
  - Farming operations
  - Pesticide use
  - Work practices
  - Lifestyle behaviors
  - Cooking practices
  - Diet history
  - Health history/ medication use
  - Reproductive health/ history (spouse)

Phase III Interviews (2005-2010)

- Applicator & Spouse
  - General information
  - Farming operations
  - Pesticide use
  - Work practices
  - Non-farm work
  - Lifestyle behaviors
  - Physical activity
  - Health history/ medication use
  - Family history
  - Reproductive health/ history (spouse)

Phase IV Questionnaires (2013-2015)

- Applicator & Spouse
  - General information
  - Farming operations
  - Lifestyle behaviors
  - Health history/ medication use
  - Family history
  - Reproductive health/ history (spouse)

- Several sub-studies (e.g. biomonitoring)

Data Collection – Follow-Up

- **Passive**
  - Linkages to administrative databases (e.g. Medicare)
  - Linkages to vital record databases (e.g. death certificates)
  - Linkages to surveillance databases (e.g. Iowa Cancer Registry)

Record Linkage

AHS applicator and spouse data

Deterministic and Probabilistic Record Linkage

Birth certificate data

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Identification of Iowa Live Births in the Agricultural Health Study

Paul A. Romitti PhD , Shinobu Watanabe-Galloway PhD , William T. Budelier MS , Charles F. Lynch MD, PhD , Soman Puzhankara MS , Donna Wong-Gibbons PhD , Jane A. Hoppin PhD & Michael C. R. Alavanja PhD

Definite match

Potential match

Non-match

Manual Review

Definite match

Undetermined

Non-match

Driver license data

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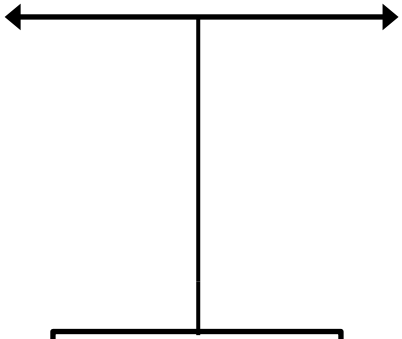
Record Linkage

AHS applicator and spouse data

(N=31,703)



Definite matches

(42,728)

Birth certificate data

(1,719,441)

METHODS

Exposure Data - Questionnaire

Name of Pesticide	Have you ever personally mixed or applied this pesticide?	How many years did you personally mix or apply this pesticide?	In an average year when you personally used this pesticide, how many days did you it?	When did you first personally use this pesticide?
Roundup, **Jury** or other **glyphosate** products	O No O Yes	O 1 year or less O 2–5 years O 6–10 years O 11–20 years O 21–30 years O More than 30 years	O Less than 5 days O 5–9 days O 10–19 days O 20–39 days O 40–59 days O 60–150 days O More than 150 days	O Before 1960 O In the 1960s O In the 1970s O In the 1980s O In the 1990s O Mark here if you used this pesticide **last year**

Paternal exposure from 6 months prior to conception through 3 months following conception

Outcomes

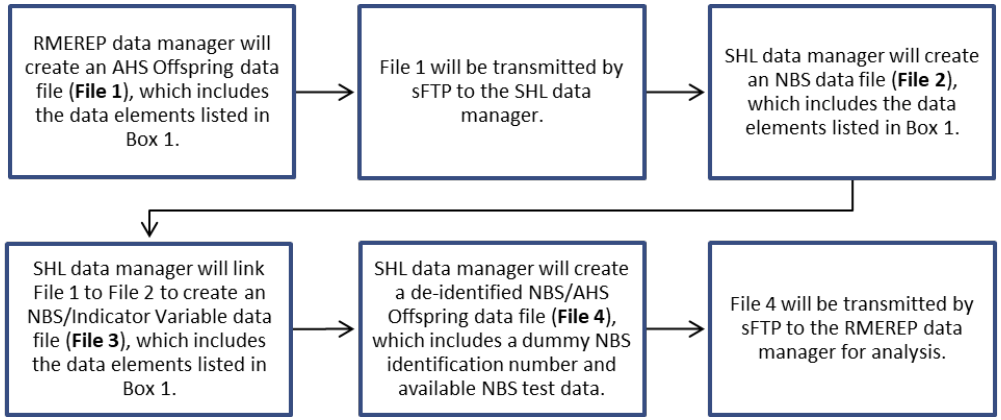
- **Create two cohorts**
  - Children of AHS applicators (AHS Cohort)
  - Children of non-AHS applicators (Non-AHS Cohort)

- **TSH screening values**

Aim 1 – Data Linkage

- **Rationale – To expand data available on the cohort of Iowa AHS participant offspring by linking cohort data to Iowa NBS data**

File 1 AHS Offspring Data	File 2 NBS Data	File 3 NBS/Indicator Data	File 4 NBS/AHS Offspring Data
AHS Identification Number	NBS Identification Number	NBS Identification Number	NBS Dummy Identification Number
Mother Name	Mother Name	Mother Name	Sex
Infant Name	Infant Name	Infant Name	Infant Anthropometrics
Birth Hospital	Birth Hospital	Birth Hospital	Parental Age, Education
Birth Date	Birth Date	Birth Date	Pesticide Exposure
Sex	Sex	Sex	Indicator Variable
Infant Anthropometrics		Indicator Variable	Selected NBS Test Data
Parental Age, Education			
Pesticide Exposure			



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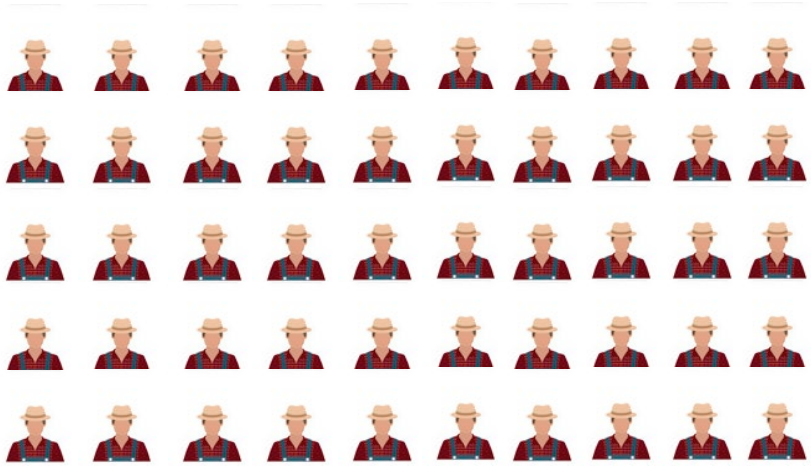
Two Study Cohorts

AHS Cohort



Non-AHS Cohort

Aim 2 – Association Analyses

- **Rationale – To examine infant thyroid function and diagnosis of primary CH using data from a large, prospective sample of agricultural workers and statewide NBS data**
- **Statistical Analysis**
  - Generate summary statistics for parental and infant characteristics, along with distributions of TSH levels, and compare these between the AHS and Non-AHS cohorts
  - Examine associations between parental use of individual pesticides and TSH levels and primary CH diagnosis using regression models adjusting for parental and infant characteristics
  - Explore cutting edge analytic methods to account for changes in pesticides used and changes in testing parameters for CH over the nearly 30-year study period

Thank You!

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