Linkages Between Agricultural Water Pollution and Health: *Why We Know So Little*

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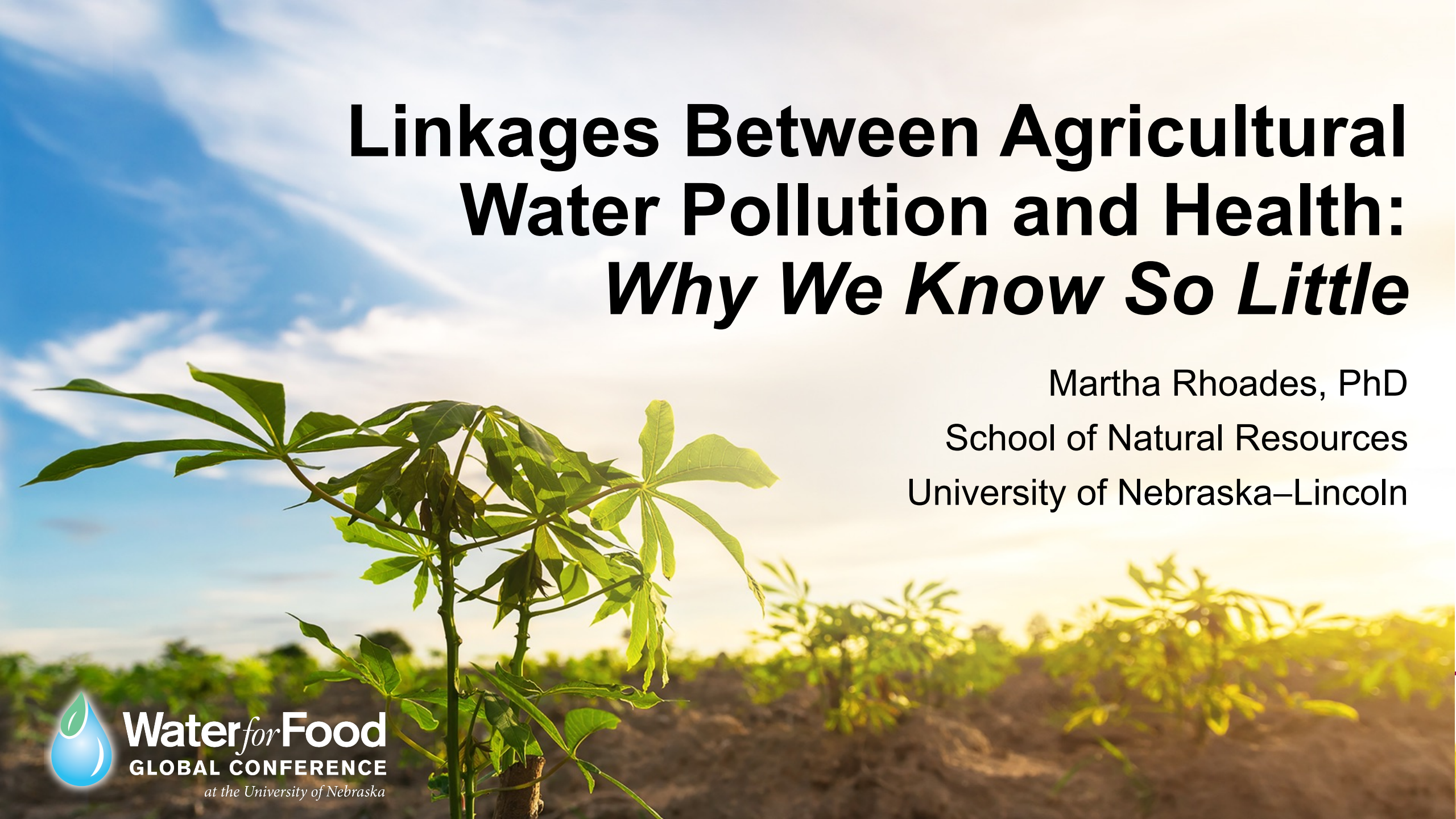

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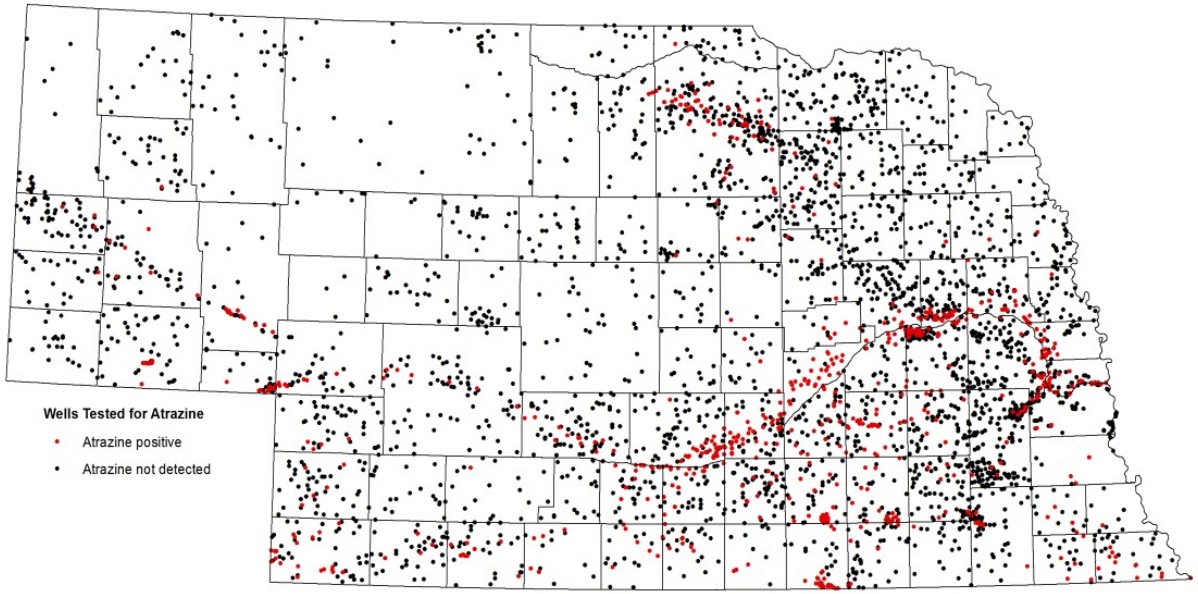
Risk Assessment

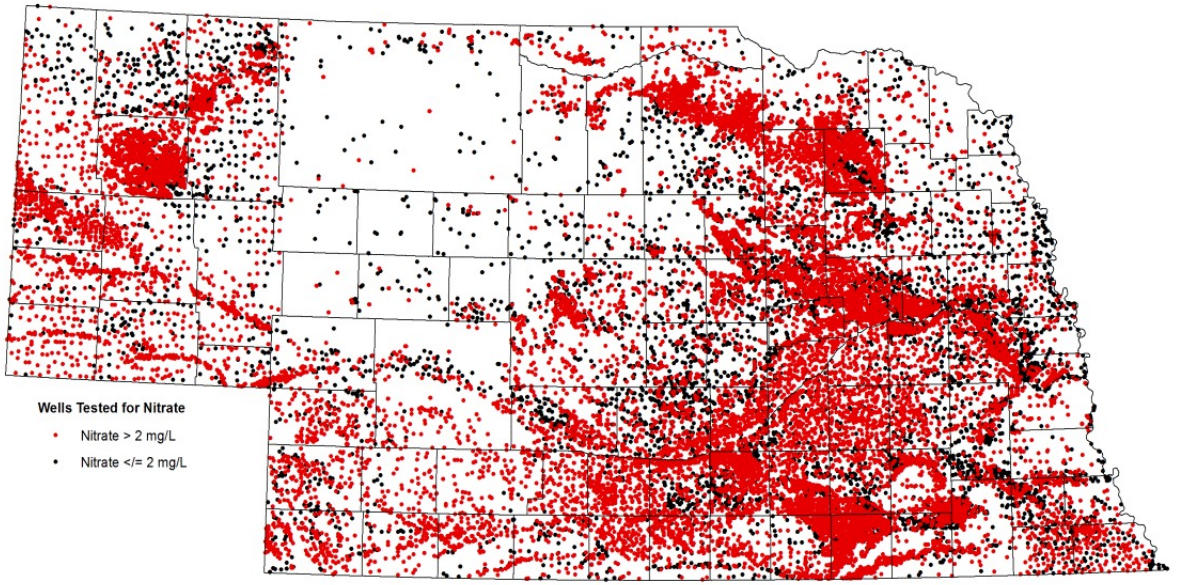
Atrazine and nitrate are the two most prevalent drinking water contaminants in Nebraska.

Does exposure increase risk of adverse health outcomes?



Wells sampled for **atrazine** (1977-2014)

916 positive of 4311 wells sampled

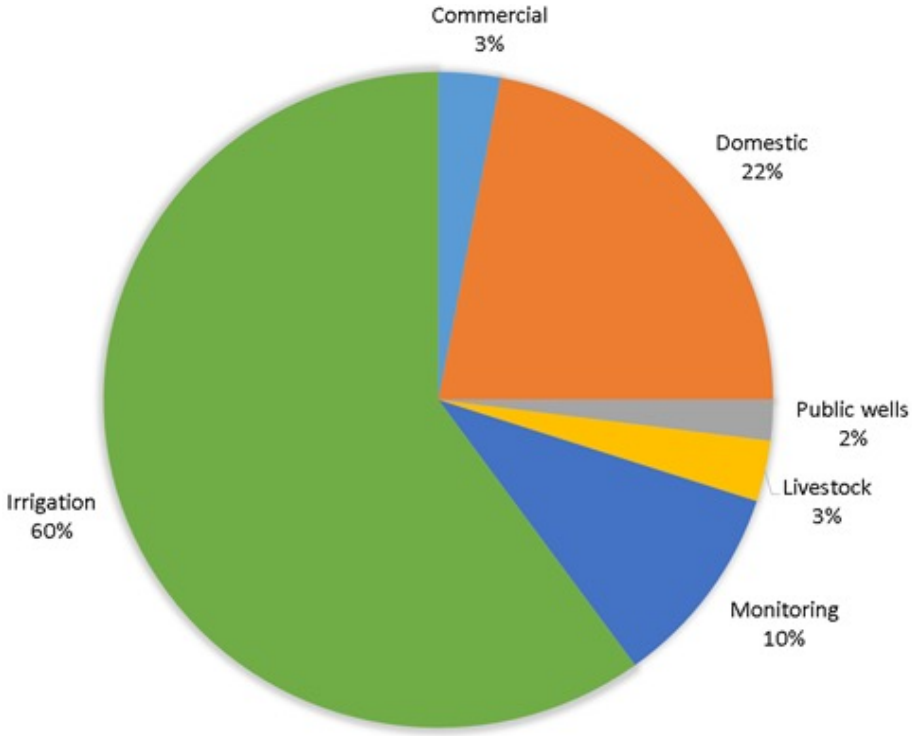


Wells sampled for **nitrate** (1977-2014)

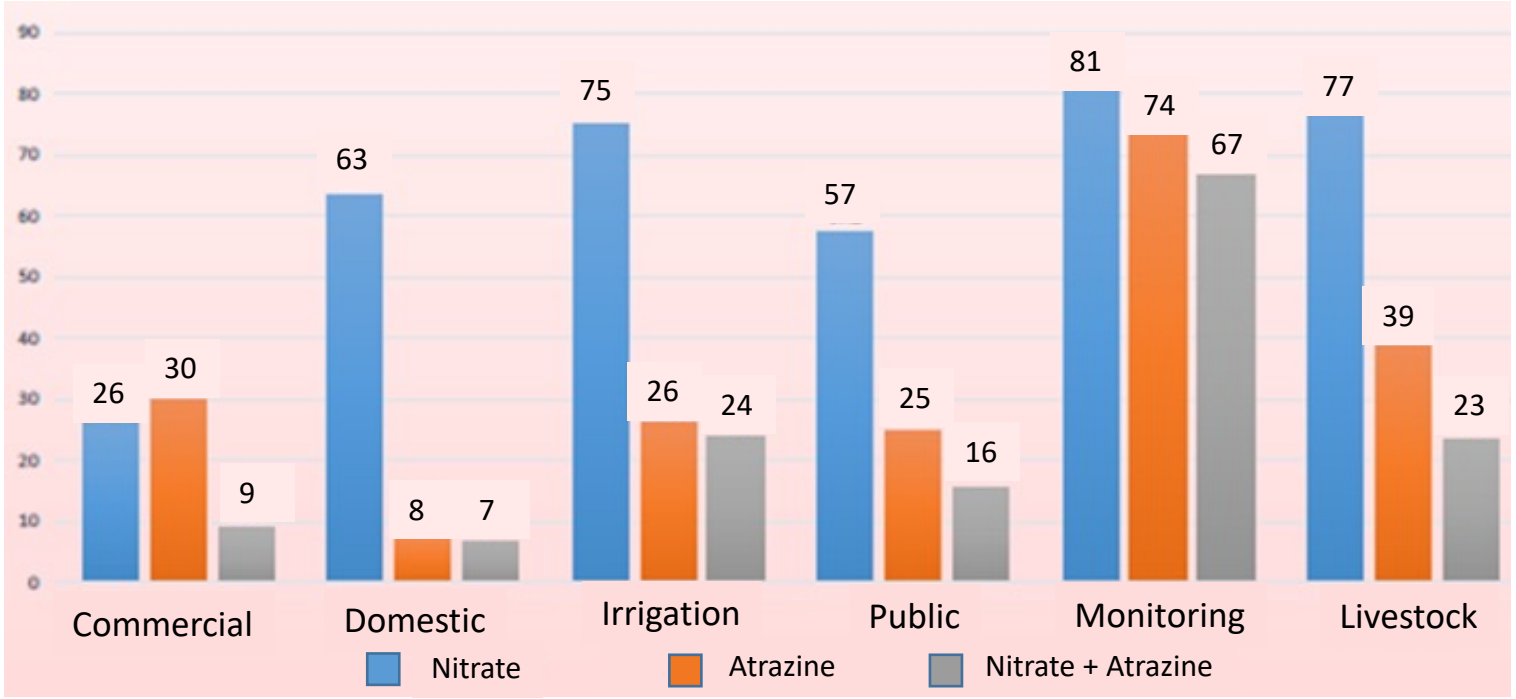
18,843 positive (> 2 mg/L) of 25,811 wells sampled

Source: Quality-Assessed Agrichemical Contaminant Database for Nebraska Groundwater (queried Fall 2015)

Agrichemical contaminated groundwater in Nebraska



Well types sampled (1977-2014)



Percent wells positive for nitrate, atrazine and combination by well type (1977-2014)

Presented at Midwest Rural Agricultural Safety and Health (MRASH) Conference November 28, 2018 by Moses New-Aaron, MPH

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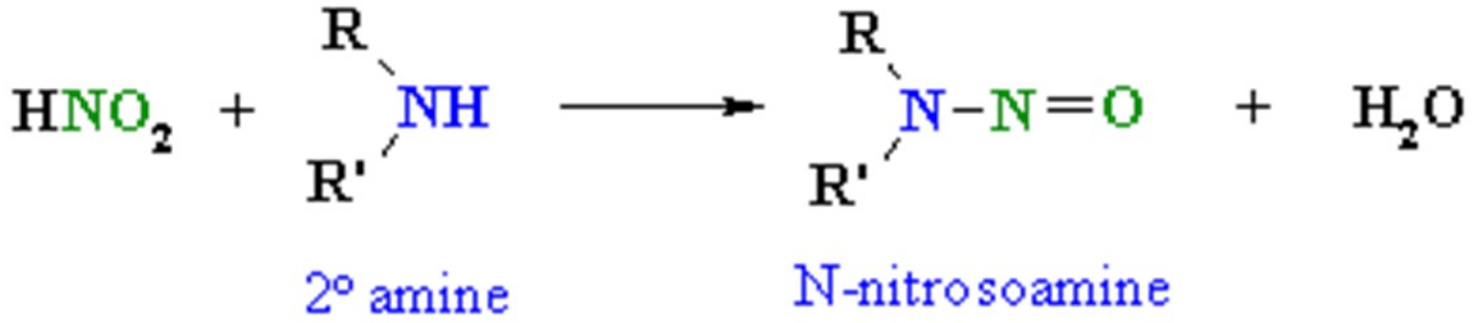
Adverse health outcomes from exposure to nitrate and atrazine in drinking water - **is it plausible?**



- Nitrate + Atrazine can form *N*-nitrosoatrazine (NNAT)
- Many nitrosamines are carcinogens/teratogens in animal models
- **Hypothesis - Exposure to the mixture is more toxic than exposure to either compound alone.**

Non-Hodgkin lymphoma risk and drinking water nitrate (and atrazine) in Nebraska

Drinking Water Nitrate and the Risk of Non-Hodgkin's Lymphoma

Mary H. Ward,[1] Steven D. Mark,[1] Kenneth P. Cantor,[1] Dennis D. Weisenburger,[2] Adolfo Correa-Villaseñor,[3] and Shelia Hoar Zahm[1]

The increasing incidence of non-Hodgkin's lymphoma (NHL) in the United States is only partially explained by known risk factors. Nitrate is a contaminant of drinking water in many rural areas. We evaluated its association with NHL after accounting for dietary nitrate intake. For 156 cases and 527 controls who used Nebraska community supplies, average nitrate exposure was estimated from 1947 through 1979. Long-term consumption of community water with average nitrate levels in the highest quartile (≥4 mg per liter nitrate-nitrogen) was positively associated with risk [odds ratio (OR) = 2.0; 95% confidence interval (CI) = 1.1–3.6]. Dietary nitrate, which came mainly from vegetables, was not associated with NHL risk, after adjusting for vitamin C and carotene intakes. Persons with a lower intake of vitamin C were at slightly higher risk of developing NHL than persons whose daily intake was ≥130 mg, for all levels of intake of drinking water nitrate; our findings were similar for the combined effect of water nitrate and carotene intake. Nitrate levels in private wells were measured at the time of the interview for 51 cases and 150 controls but were not associated with the risk of NHL after adjusting for pesticide use on the farm. These findings indicate that long-term exposure to elevated nitrate levels in drinking water may contribute to the risk of NHL. (Epidemiology 1996;7:465–471)

Keywords: non-Hodgkin's lymphoma, nitrate, drinking water, diet.

Over the past 25 years, the incidence of non-Hodgkin's lymphoma (NHL) has increased more than 70% in the United States. Rural incidence increased more rapidly than urban incidence.[1] Occupational risk factors, changes in diagnosis, and infection by the human immunodeficiency virus explain only part of the large increase in NHL incidence.[2] Pesticides have been extensively investigated as risk factors for NHL.[3–6] The herbicide (2,4-dichlorophenoxy)acetic acid (2,4-D) and organophosphate and organochlorine insecticides have

regular testing, simpler construction, and shallow well depth.

An ecologic study in Nebraska[7] indicates that elevated nitrate levels may be associated with NHL risk. County NHL incidence rates were positively correlated with the proportion of drinking water wells with nitrate levels at or above the Environmental Protection Agency (EPA) regulatory limit of 10 mg nitrate-nitrogen per liter. Nitrate is a breakdown product of nitrogen fertilizers and animal waste and may be a risk factor for cancer

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ORIGINAL RESEARCH

Atrazine and Nitrate in Public Drinking Water Supplies and Non-Hodgkin Lymphoma in Nebraska, USA

Martha G. Rhoades[1], Jane L. Meza[2], Cheryl L. Beseler[3], Patrick J. Shea[1], Andy Kahle[4], Julie M. Vose[5], Kent M. Eskridge[6] and Roy F. Spalding[7]

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Corresponding author email: mrhoades1@unl.edu

Abstract: A secondary analysis of 1999–2002 Nebraska case-control data was conducted to assess the risk of non-Hodgkin lymphoma (NHL) associated with exposure to nitrate- and atrazine-contaminated drinking water. Water chemistry data were collected and weighted by well contribution and proximity of residence to water supply, followed by logistic regression to determine odds ratios (OR) and 95% confidence intervals (CI). We found no association between NHL risk and exposure to drinking water containing atrazine or nitrate alone. Risk associated with the interaction of nitrate and atrazine in drinking water was elevated (OR, 2.5; CI, 1.0–6.2). Risk of indolent B-cell lymphoma was higher than risk of aggressive B-cell lymphoma (indolent: OR, 3.5; CI, 1.0–11.6 vs. aggressive: OR. 1.9; CI, 0.6–5.58). This increased risk may be due to *in vivo* formation and subsequent metabolism of *N*-nitrosoatrazine. A larger study is warranted to confirm our findings.

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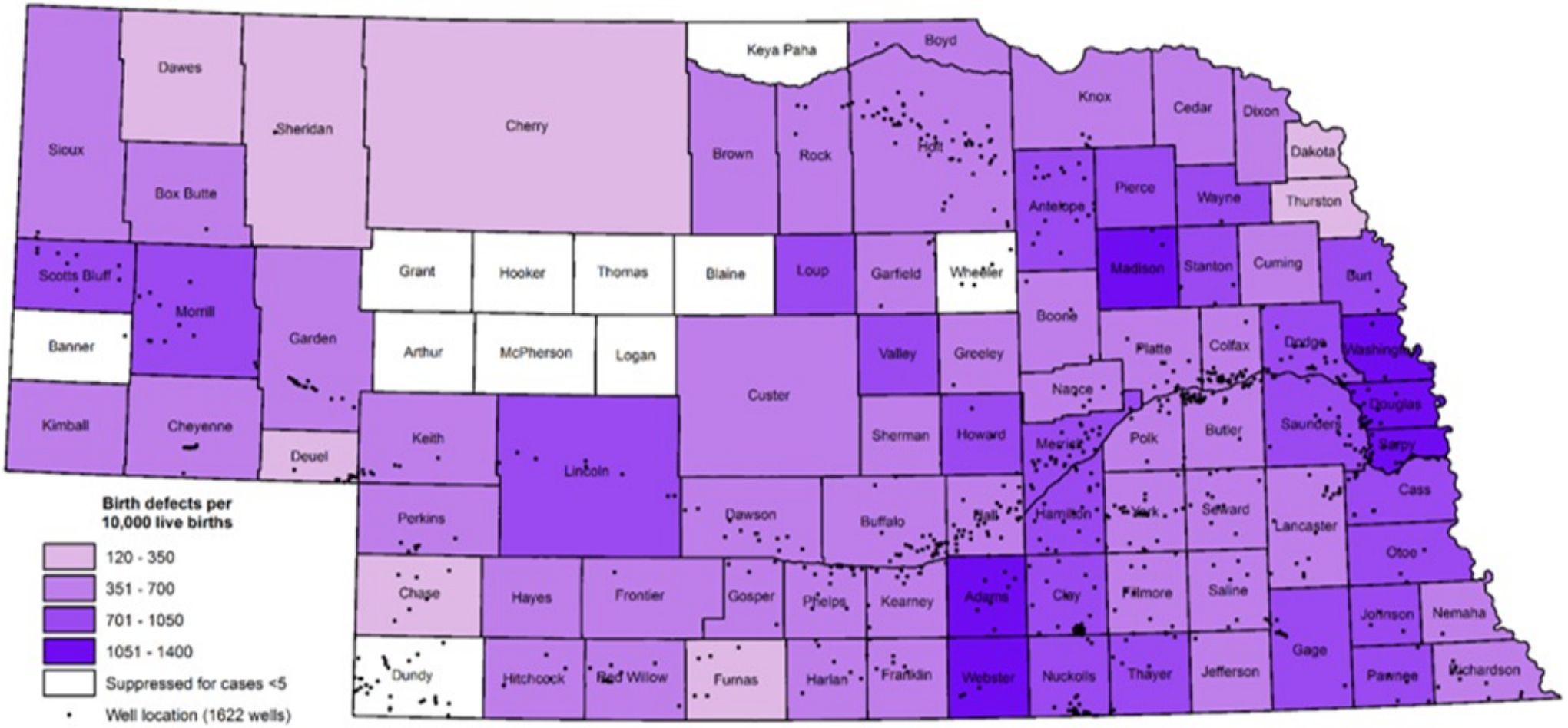
Nebraska birth defect rates by county and wells positive for nitrate + nitrosatable agrichemical



Birth defect rates 2005-2014. Source: Nebraska Department of Health and Human Services

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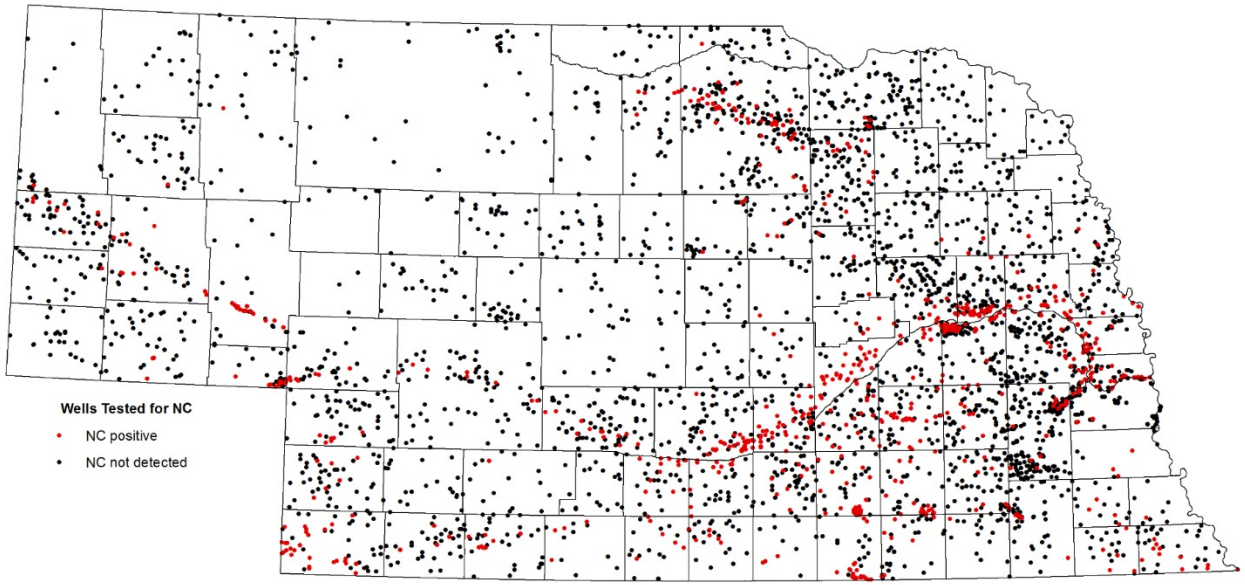
Limitations in exposure assessment

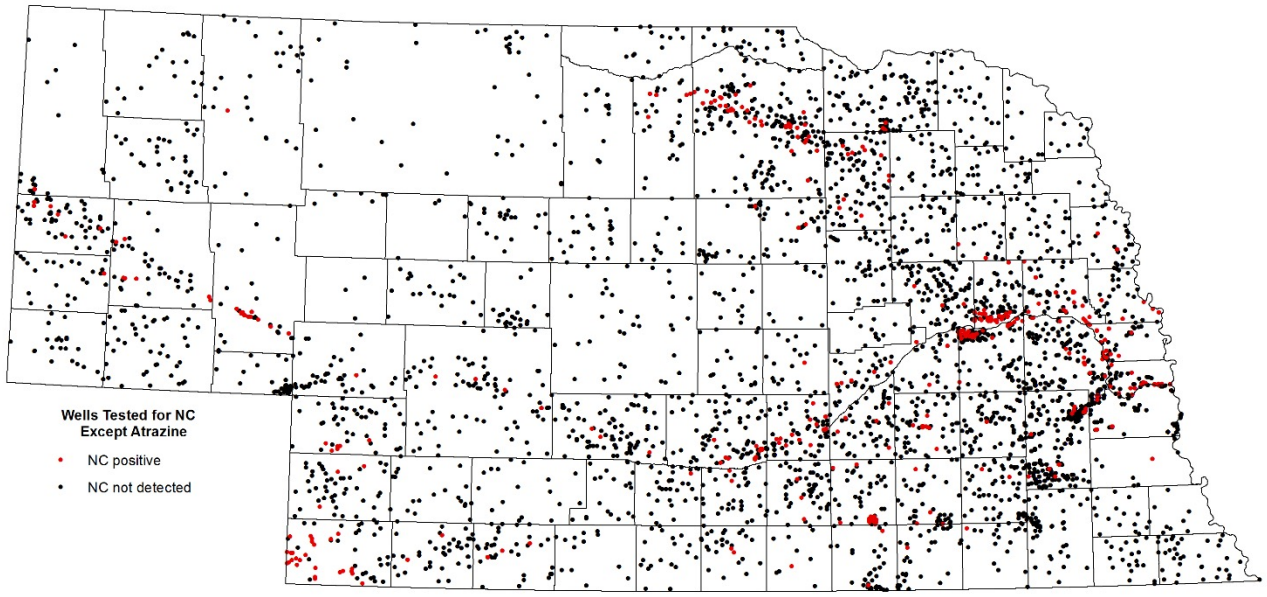
- Non-Hodgkin Lymphoma
  - Latency period
    - 10 to 20 years post exposure
  - Exposure assessment requires
    - Residential longevity
      - 10-20 years before diagnosis
    - Water quality data
      - Excludes private well users
      - Some nitrosatable agrichemicals not monitored (~ 30 in Nebraska)
- Birth Defects
  - Latency period
    - Teratogenicity occurs in first trimester
  - Exposure assessment requires
    - Residential longevity
      - 3 years prior to conception?
    - Water quality data
      - Excludes private well users
      - Some nitrosatable agrichemicals not monitored (~ 30 in Nebraska)

Nitrosatable agrichemical groundwater contaminants (NC)



Wells sampled for any NC (1977-2014)

1122 positive of 4736 wells sampled



Wells sampled for any NC except atrazine (1977-2014)

853 positive of 4736 wells sampled

Source: Quality-Assessed Agrichemical Contaminant Database for Nebraska Groundwater (queried Fall 2015)

BIRTH OUTCOMES AND WATER

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What's next?

- Pilot/feasibility case-control study
  - Nebraska women (n=40)
  - Questionnaire
    - demographics/health/residential history
  - Water sample
    - Nitrate/pesticide analysis
    - Age dating
  - Saliva sample
    - Salivary nitrate→nitrosation potential
  - Blood sample
    - Gene x Environment Interactions

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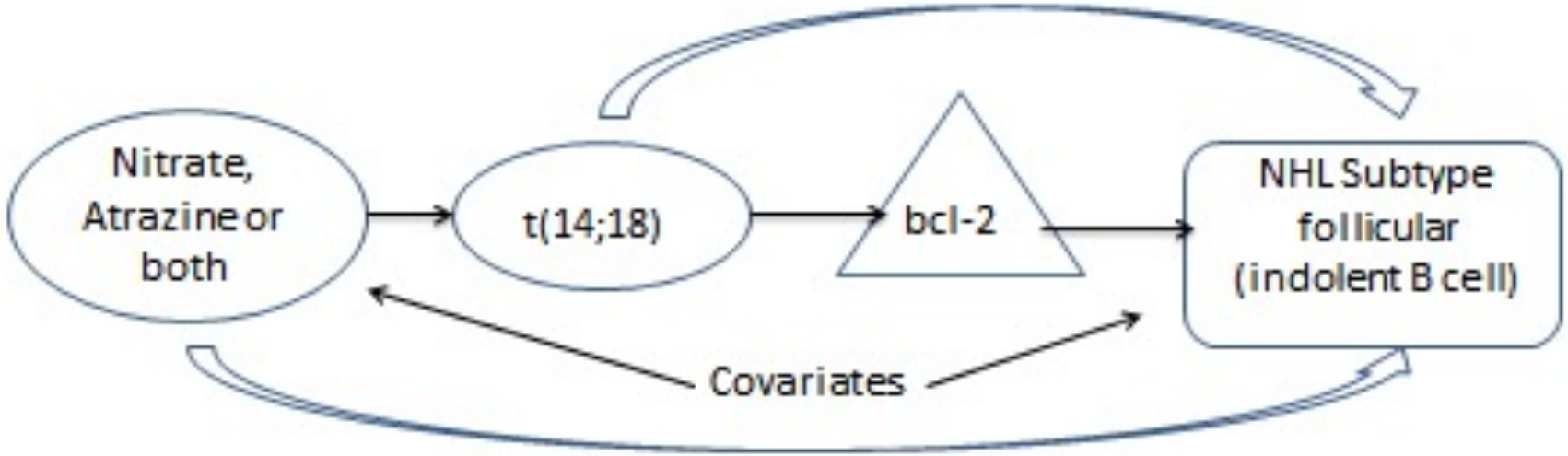
What's next?

Are individuals exposed to nitrate (NO3) and atrazine (ATZ) in drinking water at higher risk of developing t(14;18)-positive follicular NHL compared to t(14;18)-negative individuals or controls?

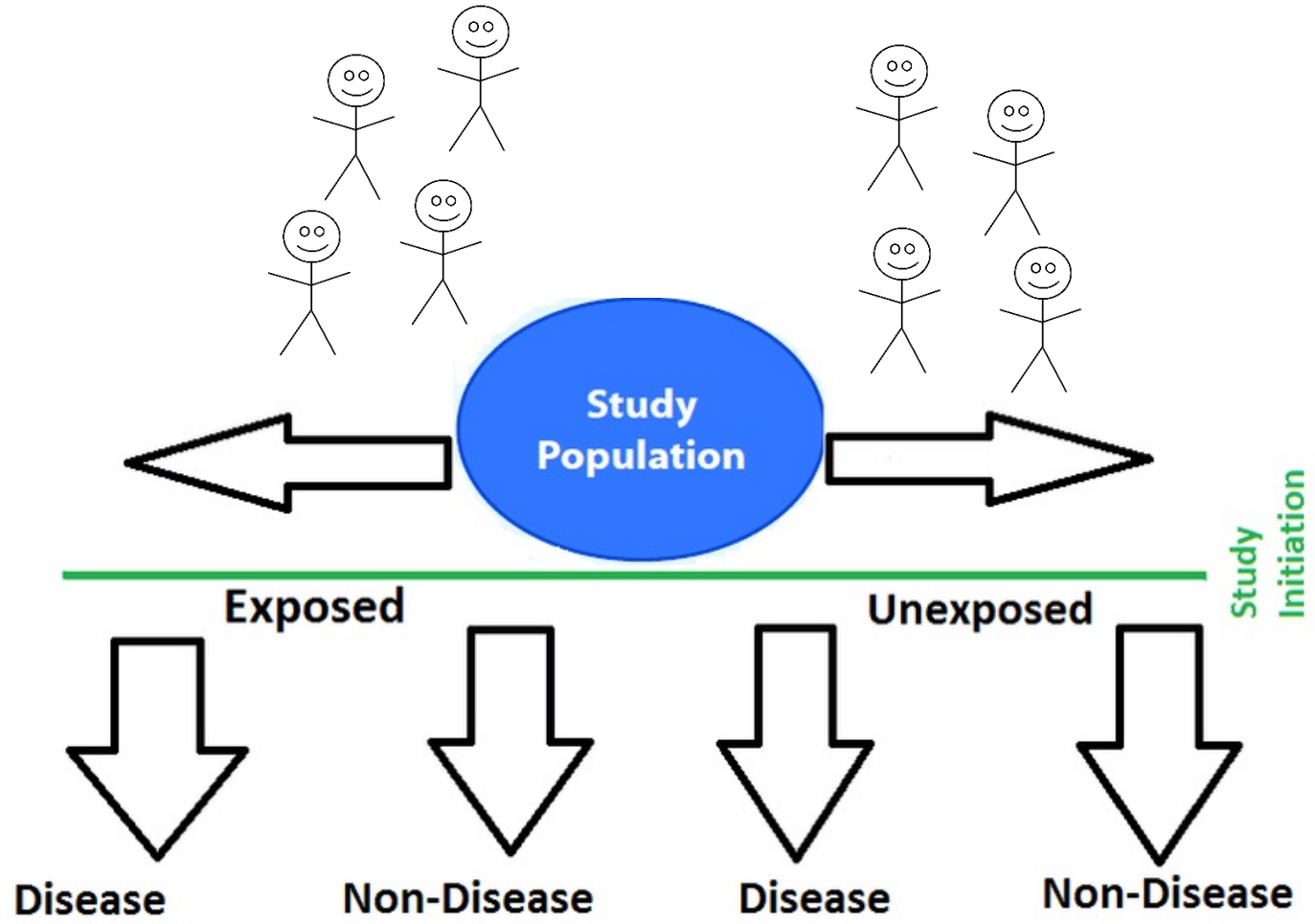


1. NO3+ATZ → follicular NHL
2. NO3+ATZ → t(14;18) positive → follicular NHL
3. NO3+ATZ → t(14;18) positive → bcl-2 → follicular NHL
4. t(14;18) → NO3+ATZ → follicular NHL
5. t(14;18) → NO3+ATZ → bcl-2 → follicular NHL

Martha Rhoades, PhD; Cheryl Beseler, PhD; Philip Bierman, MD; Patrick Shea, PhD

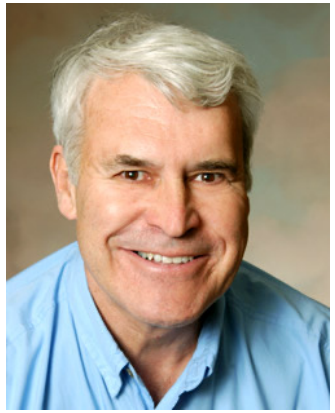
What's next?

- Nebraska may be a good venue to conduct a cohort study to better understand the human health impacts of agrichemicals in drinking water.
- If there is an association, we can develop preventive measures.



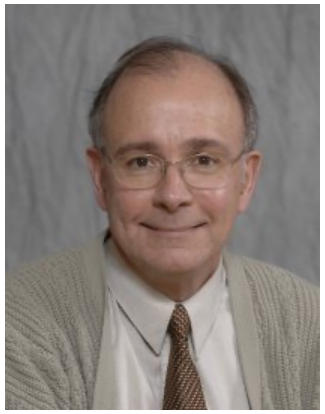
Acknowledgments

Collaboration Initiative Seed Grant

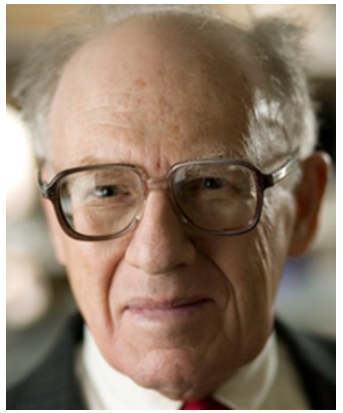


Roy Spalding, PhD

Jane Meza, PhD



Patrick Shea, PhD



Sidney Mirvish, PhD.
1929-2015