Birth Outcomes and Water

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BIRTH OUTCOMES AND WATER

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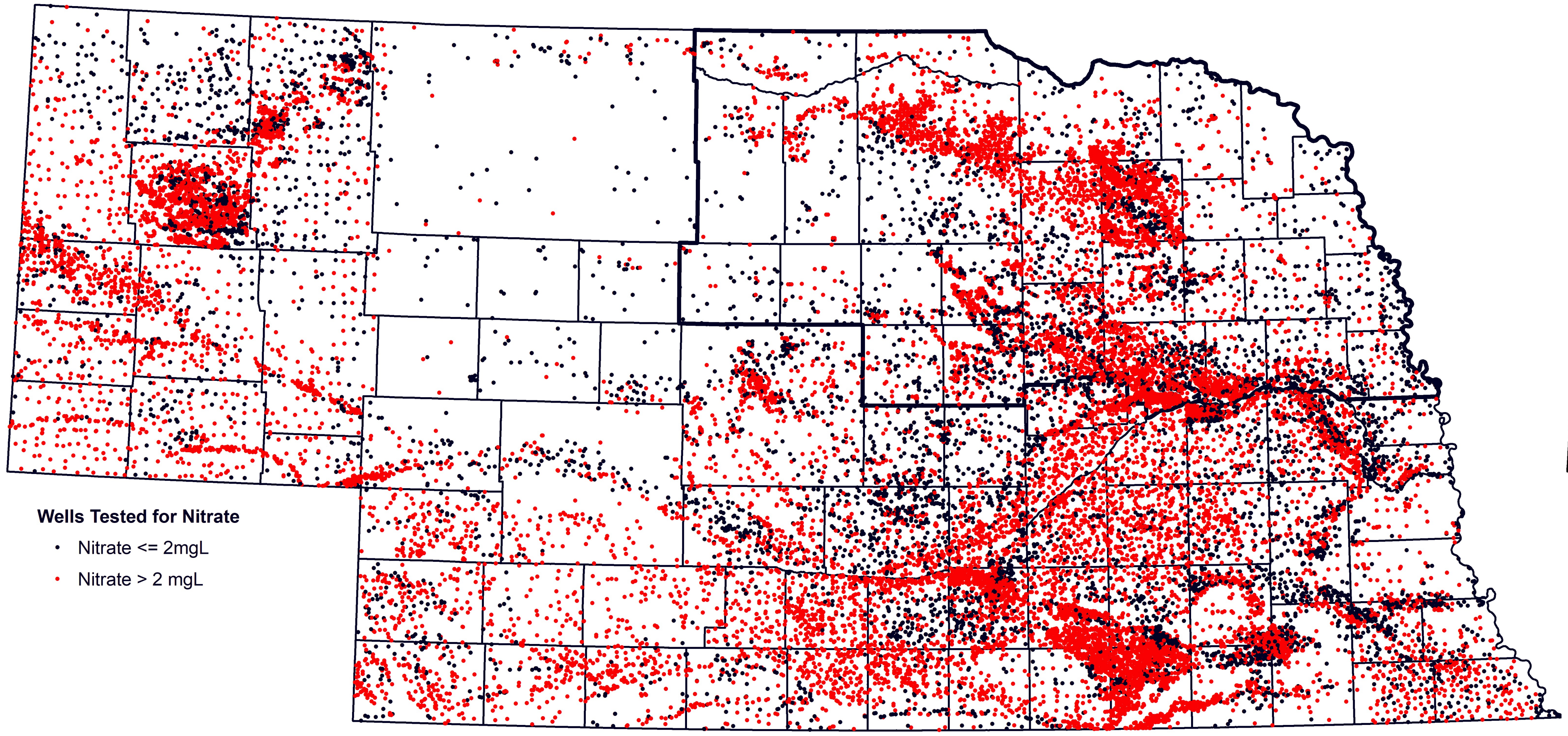
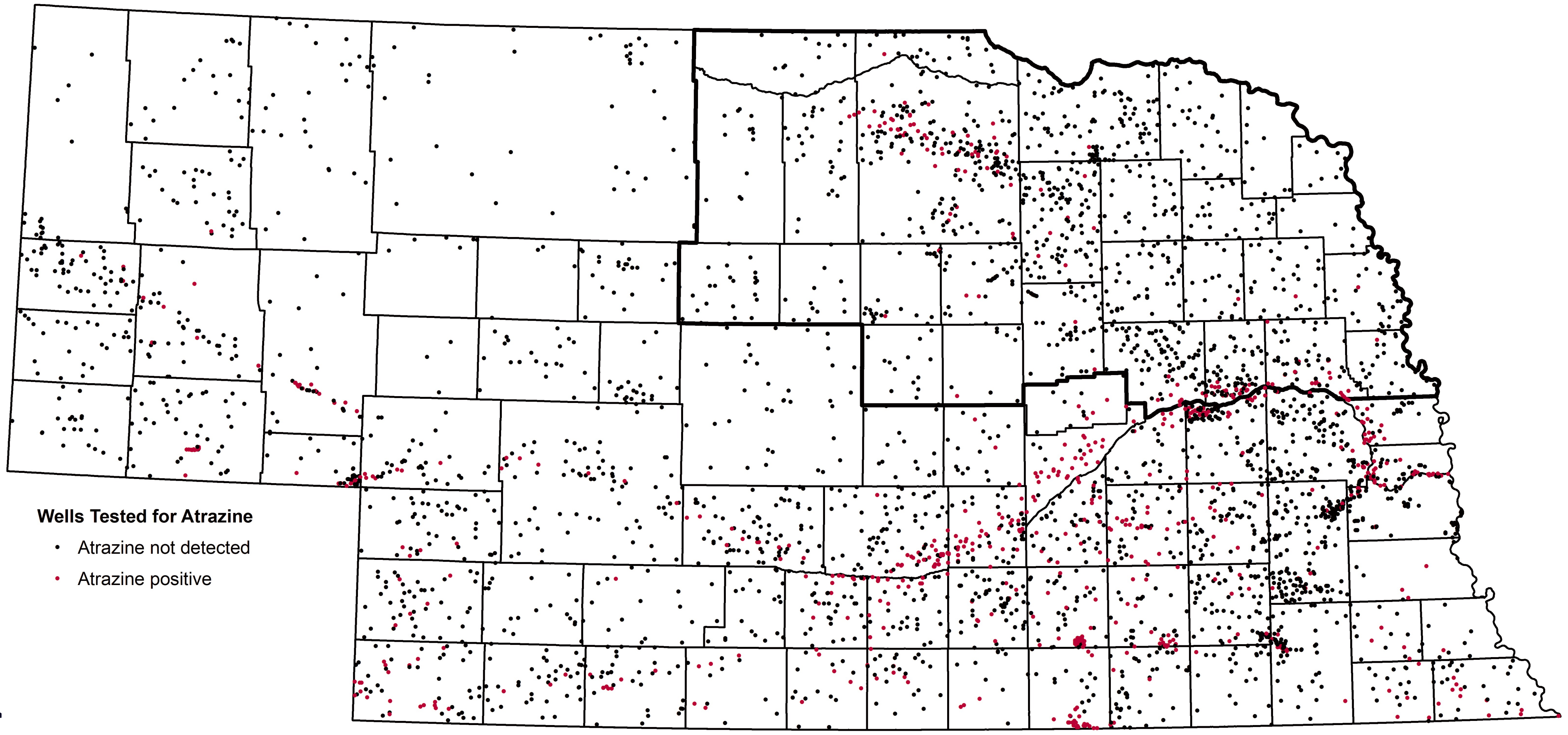
Nitrate and atrazine are the two most prevalent drinking water contaminants in Nebraska.

Does exposure increase risk of adverse health outcomes?



Wells sampled for **nitrate** (1977-2014)
70% positive (mean > 2 mg/L) of 26,447 wells sampled

Northeast CSD Service Area **nitrate**
69% positive (mean > 2 mg/L) 6,738 wells sampled



Wells sampled for **atrazine** (1977-2014)
31% positive (mean > 0 µg/L) of 4940 wells sampled

Northeast CSD Service Area **atrazine**
10% positive (mean > 0 µg/L) of 1204 wells sampled

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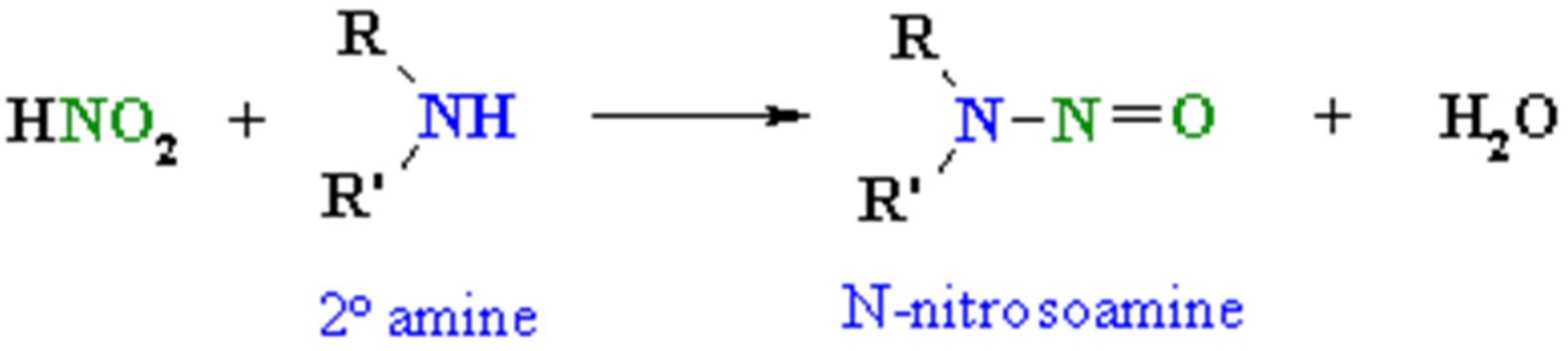
Source: Quality-Assessed Agrichemical Contaminant Database for Nebraska Groundwater (queried Fall 2015)

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



- *N*-nitrosoatrazine (NNAT) easily forms at pH similar to human stomach.
- Many nitrosamines are carcinogenic/teratogenic in animal models.
  - NNAT → chromosomal aberrations in human lymphocytes at doses 1000 X lower than nitrate or atrazine (Meisner, et al.).
- **Hypothesis – Exposure to the mixture is more toxic than exposure to either contaminant alone.**

Atrazine and nitrate in public drinking water supplies associated with non-Hodgkin lymphoma in Nebraska

	Odds Ratio	Significance	95% CI
Nitrate	0.57	0.089	0.3-1.09
Atrazine	0.96	0.84	0.66-1.4
Atz/nitrate-NHL	**2.5**	0.047	1.01-6.16
Atz/nitrate-In.NHL	**3.47**	0.044	1.04-11.51

- **NHL risk** - 2.5 times higher for subjects exposed to nitrate and atrazine in drinking water compared to subjects not exposed.
- **Indolent B-cell lymphoma risk** - 3.5 times higher for subjects exposed to nitrate and atrazine in drinking water compared to subjects not exposed.
- **Hypothesis:** Increased NHL risk due to *in vivo* formation of NNAT causing chromosomal mutations during metabolism → carcinogenesis.

Rhoades MG, Meza JM, Beseler CL, Shea PJ, Kahle A, Vose JM, Eskridge KM, Spalding RF.
Environmental Health Insights 2013:7 15-27

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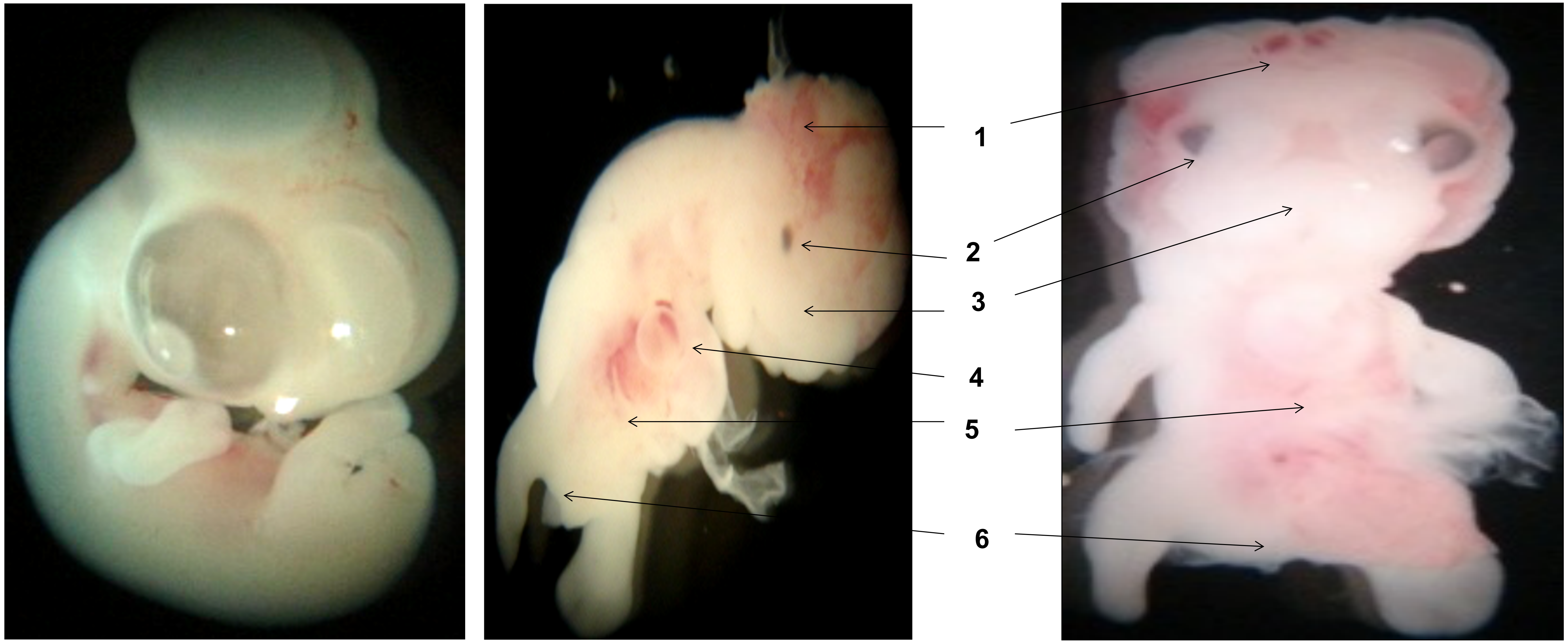
NNAT and Avian Embryo Development



Normal 5 day   NNAT 0.46 µg   NNAT 3.63 µg

1. **Neural tube defect (8%)** - neural tube fails to close
2. **Microphthalmia (11%)** - abnormally small eye
3. **Craniofacial hypoplasia (11%)** - tissue deficiency or agenesis (organ fails to develop)
4. **Heart defects (24%)** - **Ectopic heart** displacement of heart outside thoracic cavity
5. **Gastroschisis (24%)** - protrusion of abdominal contents outside the abdominal wall
6. **Caudal regression (19%)** - abnormal development of lower spine

Joshi N, Rhoades MG, Bennett GD, Wells SM, Mirvish SS, Breitbach MJ, Shea PJ
Toxicology and Environmental Health, Part A. 2013: 76(17) 1015-1022.

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Congenital Anomalies in Nebraska

- National rate: Birth defects affect about 3.3% of all live births in the U.S.
- Nebraska rate 2005-2014: 5.8%
- 600-1200 reported birth defect cases per year
    - Cardiovascular (500+)
    - Central nervous system (100+)
    - Gastrointestinal (250+)
    - Genitourinary (550+)
    - Musculoskeletal (250+)

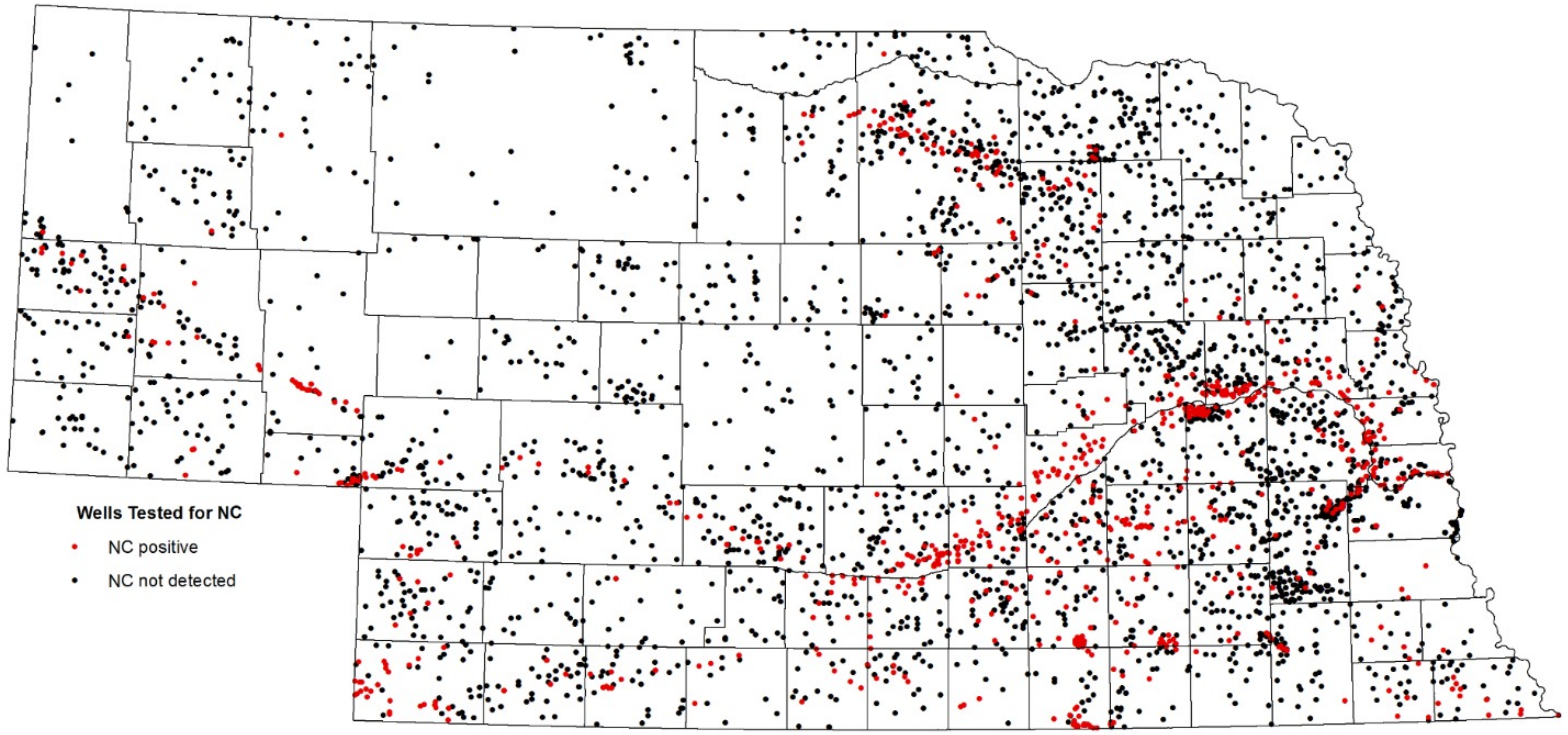
Nitrosatable agrichemicals detected in Nebraska groundwater wells

Metolachlor ESA* 70% (28; 107)	Deethyl-cyanazine 67% (4; 12)	Alachlor ESA* 52% (28; 107)	**Deisopropyl-atrazine 37% (82; 1,927)**	**Deethyl-atrazine 25% (83; 2,081)**	Alachlor ESA* 2°Amide 24% (23; 69)
Propazine 17% (66; 1,988)	Alachlor OA** 16% (19; 56)	Metolachlor OA** 12% (28; 107)	Acetochlor ESA* 11% (28; 107)	Hydroxyalachlor 11% (5; 9)	Hydroxy-simazine 8% (4; 12)
Acetochlor OA** 7% (28; 107)	Alachlor 6% (93; 4,454)	Prometon 4% (87; 2,291)	Acetochlor 3% (77; 1,591)	Bromacil 3% (74; 595)	Simazine 3% (87; 2,430)
Propachlor 2.7% (85; 2,223)	Cyanazine 2% (93; 4,451)	Metolachlor 2% (93; 4,300)	Trifluralin <1% (93; 4,186)	Ametryn <1% (62; 795)	Metribuzin <1% (93; 4,345)
Prometryn <1% (63; 797)	Butylate <1% (93; 4,300)	S-Ethyl-N,N-dipropylthiocarbamate <1% (77; 1,842)	Pendimethalin <1% (75; 1,458)		

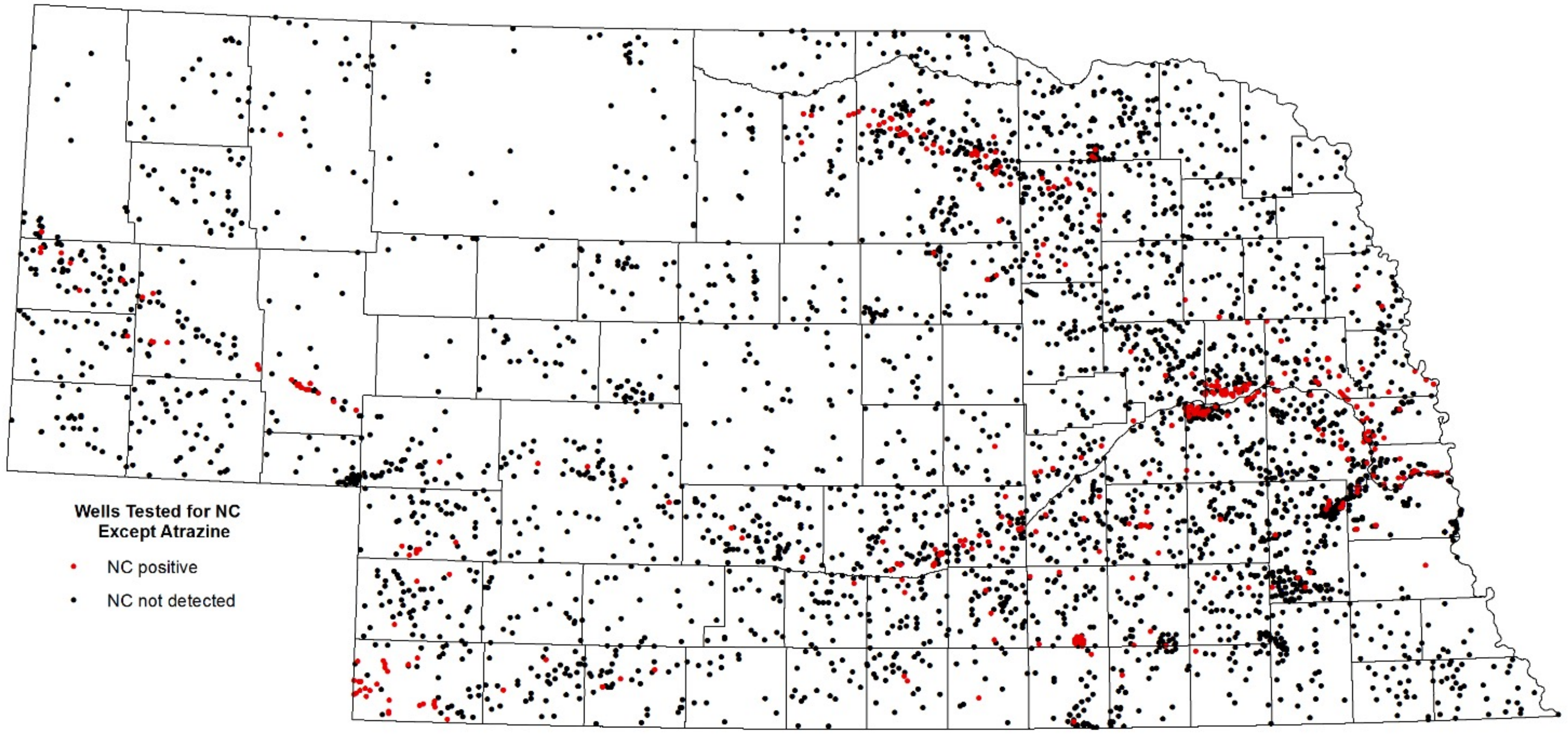
Percentage of positive wells tested for nitrate + NC
(# counties; # wells)
1,518 of 4,495 wells sampled were positive for nitrate + NC (34%)

*ethanesulfonic acid
**oxanilic acid

Nitrosatable compounds (NC) detected in Nebraska groundwater wells



Wells sampled for all NC (1977-2014)
24% positive (4736 sampled)



Wells sampled for all NC - atrazine (1977-2014)
18% positive (4736 sampled)

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

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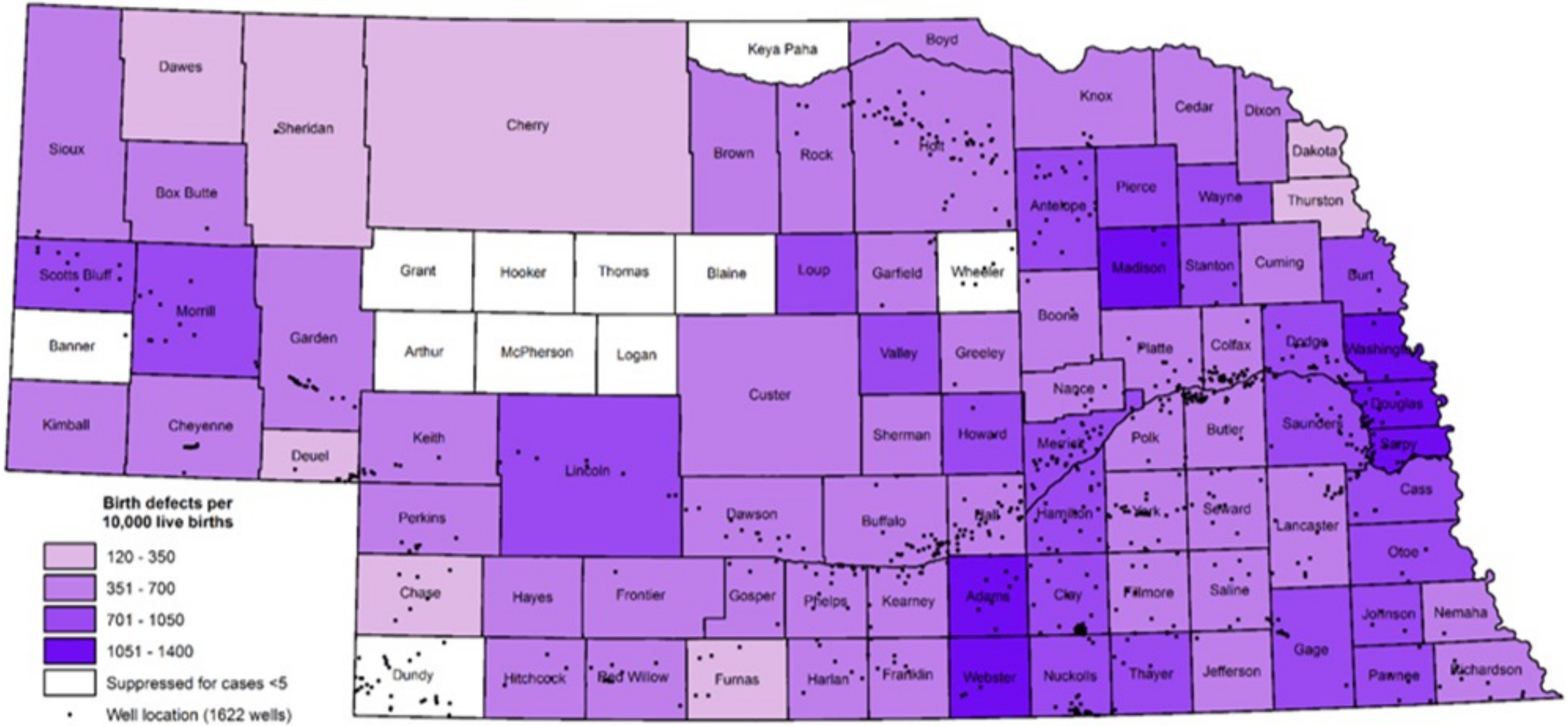
Nebraska birth defect rates by county and wells positive for nitrate + nitrosatable agrichemical



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

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

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ONGOING RESEARCH - Pilot/feasibility case-control study

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- Nebraska women (n=40; 20 cases and 20 controls)
  - 5 each water supply (public, private, bottled, other)
- Questionnaire
  - demographics/health/residential history
- Water sample
  - Nitrate/pesticide analysis
  - Age dating
- Saliva sample
  - Salivary nitrate/nitrite→nitrosation potential
- Blood sample
  - Gene x Environment Interactions
    - Genotyping for *N*-nitrosamine metabolizers (CYP2E1 and NQO1)
    - Chromosomal aberrations – t(14;18)
- Participant Perception
  - Barriers/motivation to participate

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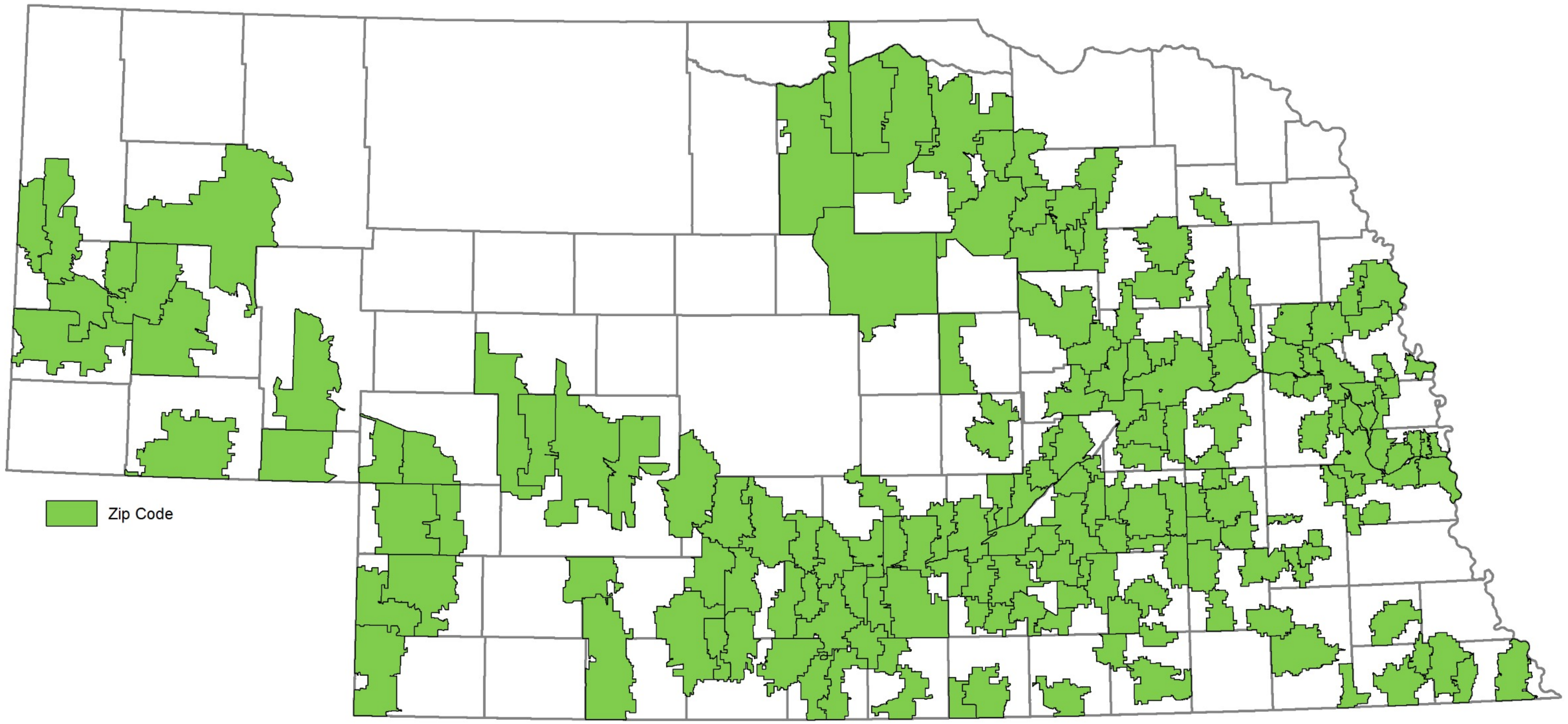
237 zip codes

- wells positive for nitrate + nitrosatable agrichemical and
- at least one birth defect case

Random sample

- 400 invites



BOW Recruitment

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Progress and opportunities

Women are all in or all out.

- Willing to be contacted?
  - Consent to be contacted does not mean consent to participate.

    Yes No

- Willing to be contacted to discuss reasons for participating or not participating?

  Yes No

Limitations

- Residential history
  - Must be a resident at current location for three years prior to conception
- Lost to follow-up
  - No response to recruitment call
  - Are these subjects also lost to the participant perception component?
- Well type
  - To date all subjects report public water system as primary drinking water source

BOW Study Challenges

- Increase awareness of issues and related research
  - Without causing alarm
  - Importance of participation in this type of study
  - Disseminating research findings to the public
- Researcher, community and stakeholder bridge
  - Partnerships
  - Public perception
  - Adapting methodology to increase participation
  - Engagement and collaboration

Acknowledgments

Participants

University of Nebraska

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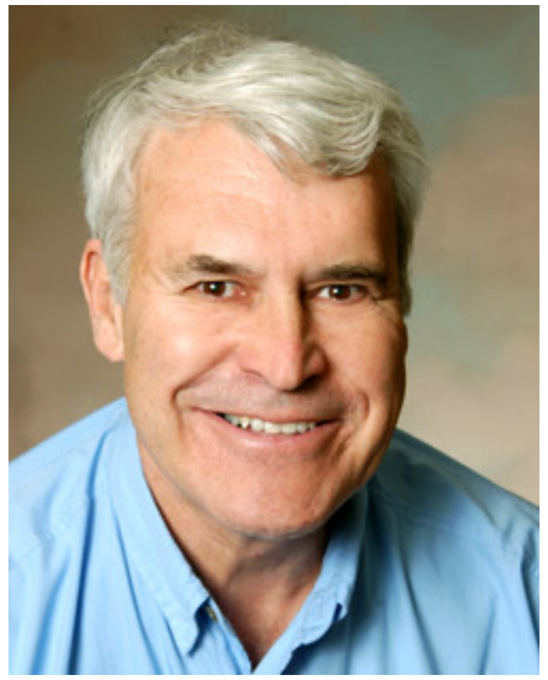

Roy Spalding, PhD

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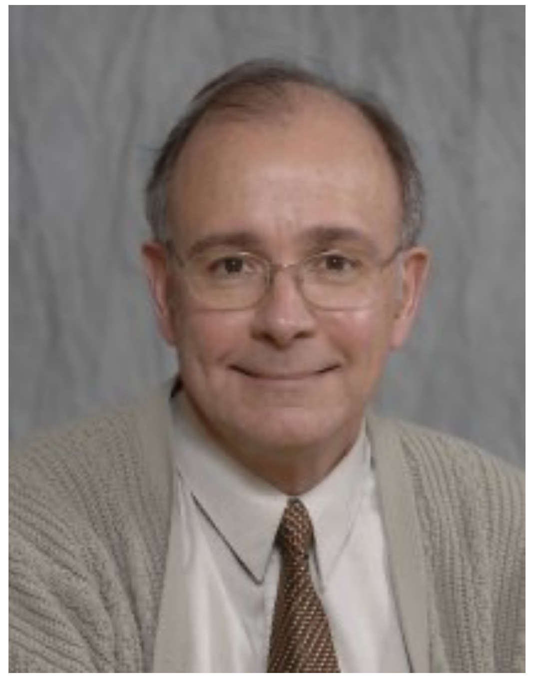

Patrick Shea, PhD

Sidney Mirvish, PhD.
1929-2015

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