

## Nitrate in Drinking Water

### What are the Health Concerns?

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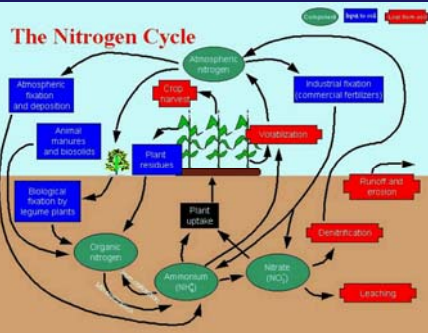


### This talk will cover...

- Nitrate in Iowa water supplies
  - Private wells overview
  - Municipal water trends
- Nitrate sources /exposure routes
  - Environmental/natural sources
- Human health concerns
  - Cancer, birth defects
- The MCL debate
  - Is 10 mg/L  $\text{NO}_3\text{-N}$  a good standard?



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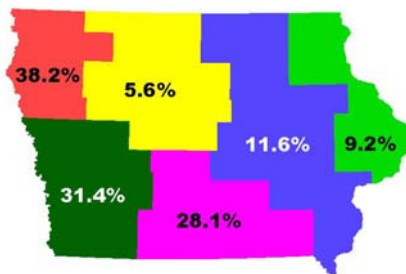
Mississippi State University  
Extension Service

### Nitrate in Iowa Water Supplies



Brian Duffy  
The Des Moines Register

### Percentage of rural wells with detections of nitrate >10 mg/l in six hydrogeologic regions in Iowa



Source: Iowa statewide rural well water survey

### Comparison of SWRL (1988–89) to SWRL2 (2006–08) Iowa Private Rural Drinking Water Wells

	SWRL 686 wells			SWRL2 473 wells		
Contaminant (MDL)*	% detections	Median Conc.*	Max Conc.*	% detections	Median Conc.*	Max Conc.*
Nitrate-N* (0.10)	58%	0.55	>100	49%	<0.10	63
Total coliform bacteria (1)	47%	<1	>16	43%	<1	>2400

\* in mg/L for nitrate-N; in MPN (most probable number) for total coliform bacteria  
\* 18% > 10 mg/L in SWRL; 12% > 10 mg/L in SWRL2



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### Nitrate in Single Source Iowa Municipal Water Supplies Using Surface Water

Decade	Dry Season		Wet Season		Dry Season		Wet Season	
	Finished Water Samples/ Mean Sites	Raw Water Samples/ Mean Sites	Finished Water Samples/ Mean Sites	Raw Water Samples/ Mean Sites	Finished Water Samples/ Mean Sites	Raw Water Samples/ Mean Sites	Finished Water Samples/ Mean Sites	Raw Water Samples/ Mean Sites
1960s	117/21 0.78	19/10 0.81	108/20 1.01	44/15 1.07				
1970s	38/17 1.12	15/13 0.42	45/23 1.66	23/14 0.76				
1980s	68/11 1.20	2/2 3.39	204/25 2.07	9/6 2.86				
1990s	307/40 2.53	3/2 4.54	332/26 3.57	1/1 2.01				

Finished Water: Dry seasons across decades: (p = 0.0034)  
Wet seasons across decades: (p = 0.0029)  
Raw Water: Dry seasons across decades: (p = 0.1633)  
Wet seasons across decades: (p = 0.1729)



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### Nitrate in Single Source Iowa Municipal Water Supplies Using Alluvial Groundwater

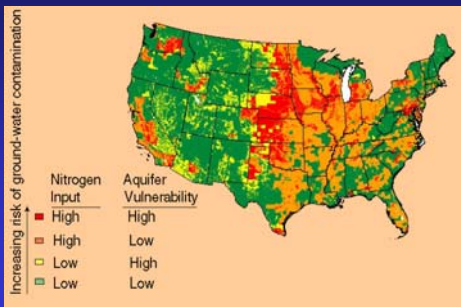
Decade	Dry Season		Wet Season		Dry Season		Wet Season	
	Finished Water Samples/ Mean Sites	Raw Water Samples/ Mean Sites	Finished Water Samples/ Mean Sites	Raw Water Samples/ Mean Sites	Finished Water Samples/ Mean Sites	Raw Water Samples/ Mean Sites	Finished Water Samples/ Mean Sites	Raw Water Samples/ Mean Sites
1960s	27/24 1.83	131/65 2.32	32/25 0.62	138/60 2.29				
1970s	79/56 4.98	130/75 2.76	71/54 6.98	164/81 2.28				
1980s	556/80 7.92	84/50 2.98	549/69 7.29	164/70 3.93				
1990s	1143/86 5.46	153/63 2.77	1313/84 5.07	84/28 4.05				

Finished Water: Dry seasons across decades: (p=0.001)  
Wet seasons across decades: (p=0.0029)  
Raw Water: Dry seasons across decades: (p=0.5737)  
Wet seasons across decades: (p=0.0114)



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### Groundwater Vulnerability to Nitrate Contamination



Map: U.S. Geological Survey

### Mean Nitrate Levels\*\* in Western Iowa Public Water Supplies by Water Source and Decade

	1980-89		1990-99		2000-08	
	Raw Water	Finished Water	Raw Water	Finished Water	Raw Water	Finished Water
Alluvium (9 PWS) (<100 ft deep)	3.6 (36)	5.2 (158)	4.9 (19)	5.7 (301)	5.5 (1)	5.4 (391)
Dakota/drift (9 PWS) (>100 ft deep)	1.1 (26)	0.9 (29)	0.66 (15)	1.4 (105)	0 (2)	1.1 (219)
Surface (8 PWS)		0.7 (59)		0.9 (120)		0.7 (104)

\*\*mg/L NO<sub>3</sub>-N  
+ (# samples)



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### Drinking Water Issues in Iowa Public Water Supplies / Private Wells

- Growth of Rural Water Systems in western and southern Iowa since late 1970s
  - Concerns about nitrate, bacteria in shallow wells
  - Safe Drinking Water Act monitoring: 10 m/L NO<sub>3</sub>-N (MCL)
    - Provide good quality water to rural areas
- ~ 450,000 Iowans use private wells for drinking water (IDNR)
  - SWRL2: bacteria (43%), ↑ nitrate (12%), arsenic (48%, 8% >0.01 mg/L)
  - Herbicide degradates: desethylatrazine 11%, acetochlor ESA 11%, alachlor ESA 27%, metolachlor ESA 33%



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### Nitrate Reduction/Removal in Drinking Water Treatment

- Mix water from a low nitrate source (deeper groundwater)
  - Surface water: seasonal differences (↑ late spring / summer)
  - Shallower groundwater sources
- Ion / anion exchange or reverse osmosis for nitrate reduction
  - DM Water Works – ion exchange
  - 4 PWS use ion/anion exchange
  - 1 PWS uses RO



graphic: Des Moines Water Works

## Drinking Water Contaminants and Health: Media Coverage



Brian Duffy  
The Des Moines Register

## Nitrate Sources and Exposure Routes

- Exogenous (environmental) nitrate
  - Food – green leafy vegetables, red meat/processed meats
  - Drinking water – surface water and ground water sources
  - Sources – fertilizers, plant residues, animal / human waste
- Endogenous (produced by body) nitrate
  - Reduction of ingested nitrate (nitrate → nitrite → N-nitroso compounds)
    - possible carcinogens, teratogens
  - Oral cavity, GI tract (mediated by bacteria)
- “Nitrosatable” drugs
  - Amine-containing drugs – more than 150 drugs can react with nitrite in the body to form N-nitroso compounds



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## Drinking Water Nitrate Exposure and Human Health

- Infant methemoglobinemia (blue-baby syndrome)
  - Hemoglobin → methemoglobin: cannot carry oxygen
  - EPA MCL: 10 mg/L  $\text{NO}_3\text{-N}$  based on blue-baby concerns
- Cancer
  - Colon cancer, bladder cancer, non-Hodgkin lymphoma ?
- Developmental effects
  - Prematurity, miscarriage, nervous system defects ?
- Other effects ?



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## Methemoglobinemia (Blue-baby Syndrome)

- Physiology of acquired condition
  - Ingested nitrate → nitrite; iron oxidizes ferric ion in hemoglobin (Hb: iron-containing  $\text{O}_2$  transport protein in blood) to ferrous state (methHb)
  - Infant gastric pH ↑ than older children/adults; ↑ intestinal flora reduces nitrate → nitrite; fetal Hb easily oxidized to methHb by nitrite than adult
  - At risk: infant formula made with high nitrate water (private wells)
  - No risk from breast-feeding where Mom consumes high nitrate water
- More a problem in Europe
  - CDC: 6 infant deaths in U.S. from 1979–96 (TX, SD, LA, VA, CO)
  - Eastern Europe: 239 cases in Poland over 14 years; Romania – 230 cases per 100,000 live births between 1990–94



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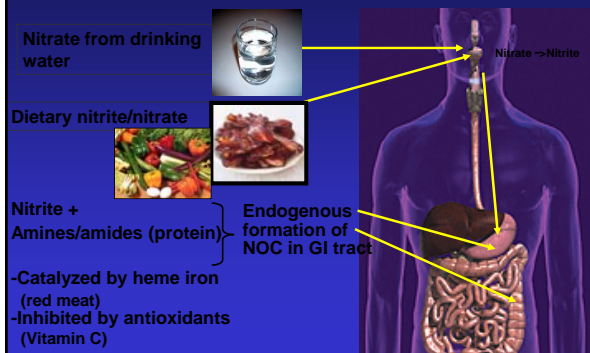
## Nitrate Metabolism in the Human Body

- Nitrate ingested via diet and drinking water
  - $\text{NO}_3$  absorbed from blood, small intestine → concentrated in saliva  $\text{NO}_3$  → secreted into upper intestinal tract
  - 25% dietary  $\text{NO}_3$  re-circulated in enterosalivary system
- Bacteria / amines in gut reduce  $\text{NO}_3$  → NOCs
- Dietary nitrate mostly excreted in urine within 24 hours



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## Endogenous formation of N-nitroso compounds (NOC) from ingested nitrate and nitrite



## Factors Affecting Endogenous Nitrosation

- Exogenous sources of nitrate
  - Green leafy vegetables, processed/cured meats
  - Water: minor source unless at high concentrations
- Inhibitors: vitamins C & E, phenolic compounds
- Catalysts: caffeine, cigarette smoke
- NOC levels depend on amino compounds, presence of bacteria /other catalysts, gastric pH, other physiologic factors
- Ingested nitrate/nitrite under conditions resulting in endogenous nitrosation is probably carcinogenic



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## Drinking Water Nitrate and Cancer Studies

- Stomach cancer – mixed results
  - No association: Netherlands study
  - Nebraska study: ↑ risk for ↑ water nitrate + ↑ processed meat intake
- Colon cancer – mixed results
  - No association: Spanish study
  - Iowa study: ↑ risk for ↓ Vit C + ↑ meat intake
- Brain cancer – mixed results
  - No association: Nebraska study
  - SEARCH Int'l study: ↑ risk for child brain tumors, ↑ nitrite in water



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## Drinking Water Nitrate and Cancer Studies

- Non-Hodgkin lymphoma – mixed results
  - No association: Iowa study
  - Nebraska study: ↑ risk >40 yrs exposure 4 mg/L NO<sub>3</sub>-N
- Bladder cancer – mixed results
  - No association: Netherlands study
  - No association: Iowa study
  - German study: ↑ risk at 13.5 mg/L NO<sub>3</sub>-N
  - Iowa study: ↑ risk at >2.46 mg/L NO<sub>3</sub>-N



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## The Iowa Women's Health Study (1998) Nitrate in Drinking Water and Cancer Risk

- 1986 survey – 42,000 women (55-69 yrs old)
  - 1989 follow-up on drinking water use: source, length of time
- 396 communities – 16,541 women, same municipal source >10 years
  - Municipal water supply nitrate data 1955-88
  - Women linked by residence town to mean NO<sub>3</sub>-N level (1955-88), no water consumption data
- Adjusted for common risk or protective factors
  - Diet, smoking, total energy, BMI, WHR, physical activity, etc.
- Adjusted for factors affecting nitrosation/nitrate exposure
  - Vitamins C & E, dietary nitrate, water supply source
- Cohort traced for cancer incidence from 1986-98



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## The Iowa Women's Health Study (1998) Nitrate in Drinking Water and Cancer Risk

Municipal water supply mean nitrate level

Primary Site	Private wells	<0.36 mg/L NO <sub>3</sub> -N	0.36–1.00 mg/L NO <sub>3</sub> -N	1.01–2.46 mg/L NO <sub>3</sub> -N	>2.46 mg/L NO <sub>3</sub> -N
Bladder	1.31 (10) 0.48–3.55	1.00 (7)	1.69 (14) 0.66–4.30	1.10 (8) 0.38–3.20	2.83 (18) 1.11–7.19
Ovary	1.55 (25) 0.77–3.13	1.00 (13)	1.52 (19) 0.73–3.17	1.81 (24) 0.88–3.74	1.84 (26) 0.88–3.84
Rectum	0.65 (23) 0.37–1.12	1.00 (33)	0.72 (25) 0.41–1.25	0.95 (32) 0.56–1.62	0.47 (16) 0.24–0.92
Uterus	1.09 (70) 0.74–1.61	1.00 (44)	0.86 (44) 0.55–1.35	0.86 (48) 0.55–1.36	0.55 (32) 0.33–0.92



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## The Iowa Women's Health Study Nitrate and Cancer Risk Reanalysis (2008)

- 20 years cancer incidence data (1987 – 2006)
  - Additional 8 years since first analysis
- Include raw water nitrate data for towns on shallow alluvial GW
  - No difference raw – finished water nitrate (Weyer et al. 2006)
  - Small number of towns – fill gaps in nitrate data timeline ?
- Recalculation of dietary nitrate levels
  - Dietary nitrate not associated with risk in 1998 study
  - More categories examined – red meat, processed meats



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### The Iowa Women's Health Study Nitrate and Bladder Cancer Reanalysis (2008)

- 86 bladder cancer cases on community water supplies
  - Additional 47 cases since 1998 analysis
  - Did not look at private well users
- Sub-analysis of bladder cancer includes disinfection by-products
  - + assoc. with bladder cancer (Villanueva et al. 2007)
  - Estimates of historical drinking water THM, HAA levels (Amy et al. 2005, AwwaRF/EPA Report)
    - Iowa study looked at surface water, groundwater supplies
    - Disinfection processes, treatment train, water chemistry
  - 59 cities with estimates of THM, HAA levels from 1955-88



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### The Iowa Women's Health Study Nitrate and Cancer Risk Reanalysis (2008)

Primary Site	<0.37 mg/L NO <sub>3</sub> -N	0.36–1.09 mg/L NO <sub>3</sub> -N	1.10–2.23 mg/L NO <sub>3</sub> -N	>2.23 mg/L NO <sub>3</sub> -N
Bladder	1.00 (15)	1.85 (24) 0.92–3.71	0.99 (16) 0.47–2.09	2.12 (31) 1.12–4.00
Ovary	1.00 (17)	2.16 (36) 1.18–3.94	2.06 (36) 1.15–3.71	2.17 (39) 1.22–3.85
Rectum	1.00 (43)	0.71 (25) 0.43–1.17	1.00 (46) 0.65–1.56	0.56 (26) 0.34–0.94
Uterus	1.00 (52)	1.21 (72) 0.82–1.78	1.05 (60) 0.71–1.55	1.00 (55) 0.67–1.47



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### The Iowa Women's Health Study Sub-Analysis: Nitrate, DBPs and Bladder Cancer (2008)

	TTHM <3.02 mg/L	TTHM 3.02-20.44 mg/L	TTHM 20.45-21.28 mg/L	TTHM >21.28 mg/L
NO <sub>3</sub> -N <0.37 mg/L	1.00 (11)	0.65 (3) 0.14–3.00	2.88 (1) 0.16–49.62	0
NO <sub>3</sub> -N 0.37-1.09 mg/L	1.00 (15)	6.11 (1) 0.70–52.83	0	0.85 (8) 0.29–2.49
NO <sub>3</sub> -N 1.10-2.23 mg/L	1.00 (4)	1.27 (4) 0.27–5.93	0	1.25 (8) 0.35–4.42
NO <sub>3</sub> -N >2.23 mg/L	1.00 (10)	3.71 (1) 0.71–19.27	0.33 (16) 0.02–5.54	1.38 (4) 0.41–4.67
NO <sub>3</sub> -N Continuous 1.11 (1.00-1.24)	1.00 (40)	1.42 (9) 0.83–2.41	2.64 (17) 0.63–10.97	1.51 (20) 0.86–2.64



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photo: www.bcbmsmt.com

### Drinking Water Nitrate – Developmental Effects

- Epidemiologic studies
  - South Australia: ↑ risk of neural tube defects (NTD), oral clefts in children whose mothers drank GW with ↑ nitrate
  - Canada: weak + association between ↑ nitrate and CNS defects
  - Sweden: weak + association between ↑ nitrate and cardiac defects
- Neural tube defects
  - Sweden: no association between drinking water nitrate and NTD
  - California: ↑ risk of anencephaly with ↑ nitrate in PWS
  - Mexican/American women: ↑ risk NTD-affected pregnancy with ↑ nitrate



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### Nitrate and Risk of Birth Defects (Exposures from Diet, Drinking Water, Drugs)

- National Birth Defects Prevention Study: Arkansas, California, Georgia, Iowa, Massachusetts, N. Carolina, New Jersey, New York, Texas, Utah
- Study of separate / joint effects of prenatal exposure to nitrate, nitrite and nitrosatable drugs on risk for selected defects
  - NTDs, limb malformations, oral clefts, heart defects
- Texas and Iowa participants periconceptual addresses (1 month pre-conception through 1<sup>st</sup> trimester) linked to community water supply systems and pertinent water nitrate sampling results



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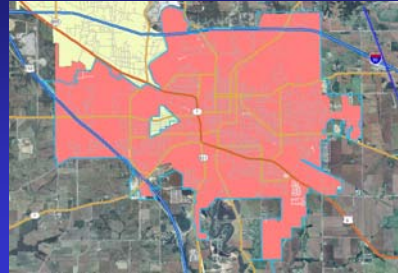
## Nitrate and Risk of Birth Defects Drinking Water Exposure Assessment

- Geocoding of mother's residences from 1 month pre-conception until end of 1<sup>st</sup> trimester
  - Layered into GIS with community boundaries
- Linkage to municipal supply distribution systems
  - Digitized maps, community boundaries, local knowledge
  - Over 1997 – 2005 time period
- Link to nitrate data for finished water sampling
  - SDWA data or utility lab data
  - Weighted averages of data closest to 4 month period



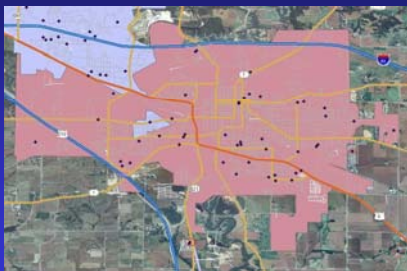
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## Exposure Assessment for Drinking Water Nitrate



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## Exposure Assessment for Drinking Water Nitrate



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## Nitrate and Risk of Birth Defects

- Project in progress
  - Data analysis through summer 2011
  - Looking at joint effects of diet, drinking water and drugs on risk
- Special studies (Texas, Iowa)
  - Nitrate concentrations in bottled water (?)
  - Modeling nitrate concentrations in private wells in Texas (Iowa?)
- Same approach for other water contaminants
  - NBDPS centers will be studying DBPs and risk
  - Linkage of geocoded addresses to PWS distribution systems, linkage to water quality data being done at CHEEC



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## Other Health Impacts of Nitrate ?

- Animal studies
  - Nitrate at high doses inhibits iodine uptake → induce thyroid hypertrophy
  - NOC can damage pancreatic beta cells (produce insulin)
- Epidemiologic studies of drinking water nitrate and childhood diseases
  - Netherlands: nitrate < MCL and ↑ risk for Type I diabetes
  - Israel: nitrate > MCL and ↑ blood pressure (dietary salt intake also a contributing factor)
  - India: nitrate > MCL and ↑ risk for acute respiratory infections (elevated methemoglobin levels also a factor)



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## The Nitrate MCL Debate



Steve Liss/Time Life Pictures/  
Getty Images

## The Nitrate MCL Debate

- EPA standard (10 mg/L NO<sub>3</sub>-N) based on methemoglobinemia
  - Other health effects research (cancer, developmental outcomes) mixed
- What are critical factors that contribute to methemoglobinemia ?
  - Nitrate in drinking water, diarrhea, GI inflammation, GI infection
  - Is nitrate causal, or does it exacerbate the condition?
- Increase MCL to 15 or 20 mg/L
  - Research inconclusive; would save on costs for measures re: nitrate pollution
- Lower MCL to 5 mg/L
  - Based on same health effects research



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## The Nitrate MCL Debate

- Interdisciplinary discussion (2005) led to these observations:
  - Handful of well-designed epi studies on drinking water nitrate and health risks among susceptible subgroups with high endogenous nitrosation
  - Epi studies found no association between dietary nitrate and cancer risk, as dietary nitrate associated with inhibitors of nitrosation (Vit C & E)
  - 2-3% of U.S. population could be exposed to ↑ nitrate in drinking water; health losses due to this exposure cannot be estimated
- Conclusion: "...not possible to weigh the costs and benefits from changing the nitrate standard for drinking water by considering the potential consequences for human health and the potential savings due to reduced costs for nitrate removal and prevention of nitrate pollution..."



van Grinsven H. et al.  
Environ Health, 2006 5:26

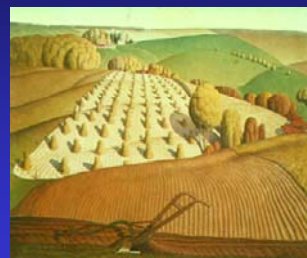
## Source Water Nitrate Trends; Future Health Research

- Nitrate trends
  - SWRL2 data: improvement in private wells – regular follow-up needed
  - Western IA PWS: shallow alluvial GW supplies – no improvement
- Health effects research needs
  - Human biomonitoring studies; endogenous nitrosation at moderate nitrate levels; examine role of precursors and modulators
  - Improve estimates of current and historical exposures; examine risk in susceptible subgroups (inflammatory bowel disease, periodontal disease)
  - Evaluate other contaminants (pesticides, DBPs, etc) that may occur along with nitrate



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## Thank You !



Grant Wood: Fall Plowing, 1931