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Anencephaly Cluster Investigation

Central Washington, 2010-2014

Advisory Committee Meeting
June 16, 2014

GOALS OF DOH ANENCEPHALY CLUSTER INVESTIGATION ADVISORY COMMITTEE

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Primary Goals

- Identify actions to prevent or reduce the likelihood of neural tube defects in the area
- Identify ways to improve reporting of neural tube defects to better ascertain rates of occurrence
- Determine if additional investigation should be conducted to assess potential exposures, and what specifically is recommended as next steps

BACKGROUND OF INVESTIGATION

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August - November 2012

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- Defined investigation area as Yakima, Benton, and Franklin counties
- Contacted CDC for technical assistance
- Performed active surveillance Nov 2012

Case Definition

- ICD-9 code: 740, 741, 742, 655.0
- Confirmed diagnosis: ultrasound or pathology report
- Resident: Yakima, Benton, or Franklin counties at time of conception
- Last menstrual period: August 2009 – present

Active Surveillance

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- Reviewed medical records of all suspect cases to validate the diagnosis

Accepted Risk Factors for Neural Tube Defects (NTDs)

- Folic acid insufficiency
- Obesity
- Diabetes
- Hispanic Ethnicity
- Selected medications
- Previous neural tube defect-affected pregnancy
- Hyperthermia

Initial Findings

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- 27 cases of NTD from January 2010-January 2013:
  - 23 anencephaly, 3 spina bifida, 1 encephalocele
- Rates:
  - Anencephaly: 8.4/10,000 vs US 2.1/10,000*
  - Spina bifida: 1.3/10,000 vs US 3.5/10,000*

*Parker SE, 2010

Dec 2012-January 2013

- Worked with CDC to develop protocol for case-control investigation
- Set up logistics for investigation team
- Notified health care providers about investigation
- Conducted study with additional CDC support in February 2013

INVESTIGATION:
CASE CONTROL STUDY

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Case-control study protocol

- Visit prenatal clinics in the three-county area
- Randomly select 4 healthy pregnancies for each NTD-affected pregnancy (108 healthy pregnancies total)
- Match to NTD-affected pregnancies by **MONTH** and **YEAR** of last menstrual period

Control selection criteria

- Healthy pregnancy defined as no indication of a birth defect (ICD 9 code 740.0-759.9)

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- Healthy pregnancy defined as no indication of a birth defect (ICD 9 code 740.0-759.9)
- Last menstrual period occurring between August 2009 through January 2013 (matched to each case)
- Residence at time of last menstrual period in Yakima, Benton, or Franklin counties

Medical Record abstraction

- Sociodemographics
- Smoking and alcohol use
- Pregnancy health conditions - diabetes, anemia, infectious diseases
- Pregnancy history
- Medication use (Rx,OTC,vitamins,folic acid)
- Pre-pregnancy height/weight
- Residential address

Additional data sources

- Birth, death and fetal death certificates, including parent occupation
- Parcel data from County Tax Assessor to establish public or private water systems
- Water quality data to examine nitrate levels in public water system

February 2013-July 2013

- Data entry from investigation
- Data cleaning and analysis
- Press release of results (July 2013)
- Draft, clear and publish official investigation findings in Morbidity, Mortality Weekly Report (MMWR Sept 6, 2013: 62(35);728)
- Outreach to local health care providers

CASE CONTROL RESULTS

Maternal Characteristics

	Cases (N=27)	Controls (N=108)	OR (95% CI)
County of Residence			
Benton	9 (33%)	31 (29%)	1.3 (0.5, 3.2)
Franklin	3 (11%)	12 (11%)	1.1 (0.3, 4.3)
Yakima	15 (56%)	65 (60%)	Reference
Hispanic	15 (60%)	55 (51%)	1.4 (0.6, 3.4)
Non-Hispanic	10 (40%)	52 (49%)	Ref
HS or less	16 (76%)	66 (62%)	2.0 (0.7, 5.8)
Some college/degree	5 (23%)	41 (38%)	Ref
Overweight/Obese	13 (50%)	66 (61%)	0.6 (0.3, 1.5)
Underweight/Normal	13 (50%)	42 (39%)	Ref
Public health insurance	17 (65%)	68 (65%)	1.0 (0.4, 2.5)
Private health insurance	9 (35%)	37 (35%)	Ref
Mexico born	5 (21%)	32 (30%)	0.6 (0.2, 1.8)
US born or other	19 (79%)	76 (70%)	Ref
Mean age (SD)	26.0 (5.9)	28.2 (5.9)	t-test p< .10

Pregnancy Risk Factors

	Cases (N=27)	Controls (N=108)	OR (95% CI)
Drank alcohol	3 (11%)	17 (16%)	0.7 (0.7, 2.4)
Did not drink alcohol	24 (89%)	90 (84%)	Ref
Smoker	2 (7%)	8 (7%)	1.0 (0.2, 5.0)
Non-smoker	25 (93%)	100 (93%)	Ref
Anemic	2 (8%)	29 (28%)	0.2 (0.0, 1.0)
Not anemic	23 (92%)	73 (72%)	Ref
Diabetes	3 (11%)	12 (11%)	1.0 (0.3, 3.8)
Non-diabetic	24 (89%)	96 (89%)	Ref
Infections while preg	10 (37%)	30 (28%)	1.5 (0.6, 3.7)
No infections while preg	17 (63%)	78 (72%)	Ref
At least 1 previous preg	19 (70%)	84 (78%)	0.7 (0.2, 2.0)
No previous preg	8 (30%)	24 (22%)	Ref
At least 1 previous birth	17 (63%)	79 (73%)	0.6 (0.2, 1.7)
No previous birth	10 (37%)	29 (27%)	Ref
Private well	6 (23%)	19 (18%)	1.4 (0.5, 3.9)
Municipal water	20 (77%)	88 (82%)	Ref

Early Pregnancy* Vitamin/Medication Use

	Cases (N=27)	Controls (N=108)	OR (95% CI)
No folic acid suppl Folic acid suppl	21 (78%) 6 (22%)	98 (91%) 10 (9%)	0.4 (0.1, 1.1) Ref
Folic acid adjusting for Hispanic ethnicity			0.3 (0.1, 1.1)
No prenatal vit Prenatal vit	23 (85%) 4 (15%)	93 (86%) 15 (14%)	0.9 (0.3, 3.1) Ref
Opioid use No opioid use	1 (4%) 26 (96%)	2 (2%) 106 (98%)	2.0 (0.2, 23.4) Ref
Antidepressant use No antidepressant use	1 (4%) 26 (96%)	2 (2%) 106 (98%)	2.0 (0.2, 23.4) Ref
Antibiotic use No antibiotic use	1 (4%) 26 (96%)	4 (4%) 104 (96%)	1.0 (0.1- 9.3) Ref
Took contraceptives No contraceptives	1 (4%) 26 (96%)	3 (3%) 105 (97%)	1.3 (0.1, 13.5) Ref

* Early Pregnancy defined as between LMP & LMP + 6 weeks

Conclusions

- No clear associations.
- No statistically significant differences between cases and controls, although study had low power.
- Overall low early pregnancy folic acid use in both case and control groups
- PRAMS Survey data 2009-2011:
  61% no early preg folic acid 3-county area
  50% in the rest of Washington State

Limitations

- Study had low statistical power to detect an association
- Limited information on exposures occurring at time of neural tube formation (4 weeks after conception)

FOLLOW UP

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March 2013-Present

- Tracked new cases diagnosed since January 2013
- Used passive surveillance with active follow up among area hospitals and prenatal clinics
- Requested medical records for review
- Obtained birth, death and fetal death certificates from vital statistics

March 2013-Present

- Briefed public health leadership of investigation findings
- Provided outreach to health care providers & public
- Prepared updated press releases
- Responded to inquiries from public & held listening sessions to learn concerns
- Conducted media interviews

OVERVIEW OF FINDINGS

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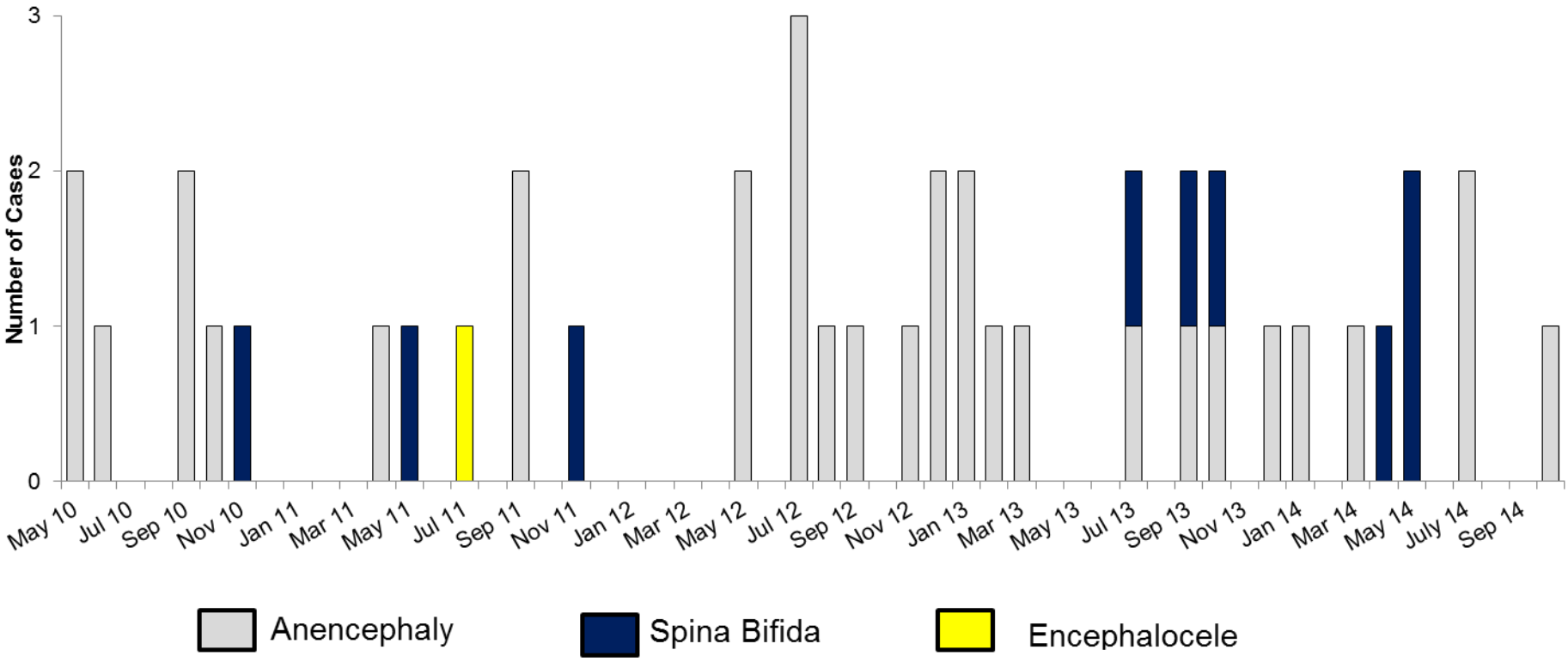
Neural Tube Defects by Month of Estimated Delivery Date*



*Estimated Delivery Date uses Delivery date for gestational age> 37 weeks and Estimated Delivery Date for gestational age< 37 weeks at delivery

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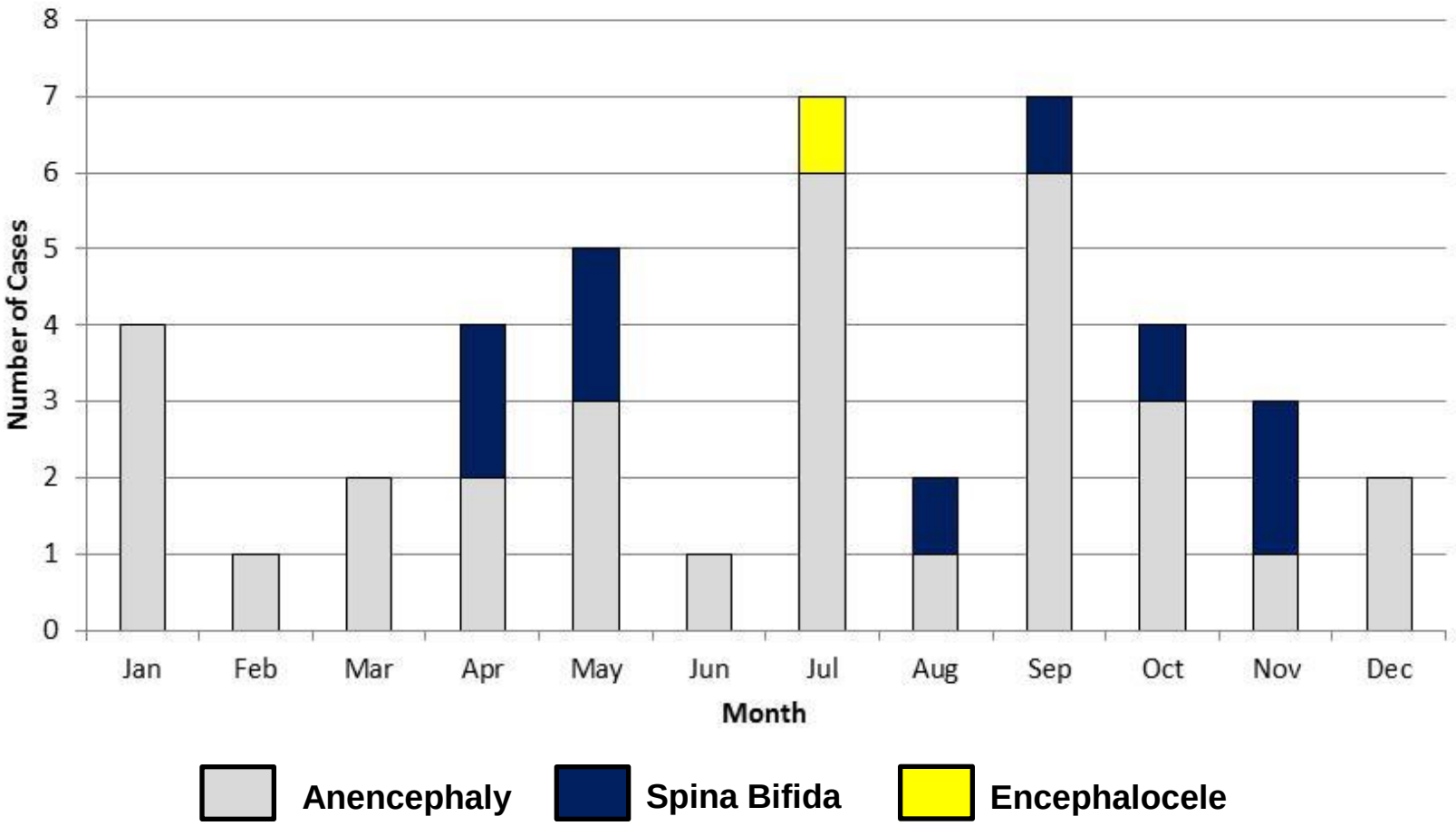

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Neural Tube Defects by Year of Delivery or Estimated Year of Delivery[1]

	Number	Total births	Rate per 10,000 births	95% CI
All Neural Tube Defects				
2010	7	8565	8.2	(3.3, 16.8)
2011	6	8528	7.0	(2.6, 15.3)
2012	9	8352	10.8	(4.9, 20.5)
2013	12	8084	14.8	(7.7, 25.9)
2014	8	na		
Total to date[2]	42	na		
Anencephaly				
2010	6	8565	7.0	(2.6, 15.2)
2011	3	8528	3.5	(0.7, 10.3)
2012	9	8352	10.8	(4.9, 20.5)
2013	9	8084	11.1	(5.1, 21.1)
2014	5	na		
Total to date[2]	32	na		

[1] Estimated year of delivery is used for cases terminated or delivered before 37 weeks gestation.

[2] Total to date reflects cases confirmed by June 6, 2014 with a delivery or estimated date of delivery in 2010-2014.

Neural Tube Defects by County of Residence

	Total Number[1]	Number 2010-2013	2010-2013 births	Rate per 10,000 births	95% CI
All Neural Tube Defects					
Benton County	17	14	10,171	13.8	(7.5, 23.1)
Franklin County	6	5	6,698	7.5	(2.4, 17.4)
Yakima County	19	15	16,660	9.0	(5.0, 14.9)
3 County Area	42	34	33,529	10.1	(7.0, 14.2)
Anencephaly					
Benton County	15	13	10,171	12.8	(6.8, 21.9)
Franklin County	4	3	6,698	4.5	(0.9, 13.1)
Yakima County	13	11	16,660	6.6	(3.3, 11.8)
3 County Area	32	27	33,529	8.1	(5.3, 11.7)

[1] Total number reflects cases confirmed by June 6, 2014 with a delivery or estimated date of delivery 2010-2014.

Neural Tube Defects by Geography

- We have a map, but are not sharing it to protect the mothers' confidentiality
- Mothers with affected pregnancies resided across the 3-county area
- Case mothers resided in 15 of the 33 zip codes in the 3-county area
- In general, more cases from more populated areas

Neural Tube Defects by Race Ethnicity

	Total Number[1]	Number 2010-2013	2010-2013 births	Rate per 10,000 births	95% CI
All Neural Tube Defects					
Hispanic	20	18	17,435	10.3	(6.1, 16.3)
Non-Hispanic White	18	14	13,559	10.3	(5.6, 17.3)
Other	0	0	2,535	0.0	
Anencephaly					
Hispanic	16	15	17,435	8.6	(4.8, 14.2)
Non-Hispanic White	12	10	13,559	7.4	(3.5, 13.6)
Other	0	0	2,535	0.0	

[1] Total number reflects cases confirmed by June 6, 2014 with a delivery or estimated date of delivery 2010-2014. Four anencephaly cases had unknown race/ethnicity.

Neural Tube Defects by Ascertainment Method

Surveillance Type	All NTDs		Anencephaly	
	N=31	rate per 10,000	N=25	rate per 10,000
Passive Surveillance				
Vital records, GA>20 wks, discharge indices 740-740.1, 741-742.1	19	5.7	14	4.2
Passive Surveillance with Active Follow-up				
Vital records, discharge indices, review nursery log	19	5.7	14	4.2
Vital records, discharge indices, review nursery logs and OB logs, no induced abortions	20	6	15	4.5
Active Surveillance				
Vital records, discharge indices & NICU, OB, cath, lab, genetics and radiology logs	30	9	24	7.2
Complete - include prenatal clinics	31	9.2	25	7.5

Numbers reflect cases confirmed by June 6, 2014 with a delivery or estimated date of delivery 2010-2013. This excludes 11 cases (7 anencephaly) due to incomplete information or delivery date in 2014. Total Births is 33, 539.

Environmental Exposure Hypotheses considered by DOH

- Occupational and residential pesticide exposure
- Nitrates in drinking water
- Radiation from Hanford nuclear facility
- Radiation from Fukushima release

Environmental Exposure Hypotheses considered by DOH

Occupational and residential pesticide exposure:

- Few cases reported with maternal or paternal agriculture or agricultural processing occupations.
- No seasonality observed among anencephaly affected pregnancies.
- Affected pregnancies located across 3-county area.
- Affected pregnancies are not clustered near farms or agricultural fields.
- Little support in published literature for specific pesticides.

Environmental Exposure Hypotheses considered by DOH

Nitrates in drinking water:

- Most of the women's residences in the study were on public water systems (not private wells)
- Water quality was explored for public systems from 2000-2013
- Monthly mean nitrate levels for municipal systems from 2010-2013 were well below the EPA standard of 10 mg/l with most below 5 mg/l
- Methemoglobinemia suggested by community as proxy for nitrates in drinking water. In Yakima, less than 5 hospitalizations each year 2008-2013 and no infant hospitalizations.

Environmental Exposure Hypotheses considered by DOH

Radiation from Hanford Nuclear Facility:

- We have not seen change in releases from Hanford to account for a recent clustering of birth defects in the Yakima Valley or Columbia Basin.
- We don't see a pathway from which radiation from Hanford could have exposed most or all women with anencephaly-affected pregnancies.
- Leaks that seep into Columbia River are diluted and carried downstream and are unlikely to get into drinking water used by most of the women. This water is carefully monitored to assure it meets safety standards.

Environmental Exposure Hypotheses considered by DOH

Radiation from Fukushima:

- Anencephaly affected pregnancies were confirmed prior to Fukushima release in 2011 and continued after.
- No reported increase in anencephaly after Fukushima release along west coast of US

Additional concerns raised by Community Listening Sessions

- E coli
- Mold in masa flour
- Health of father
- Air quality
- Cache Valley Virus
- Depleted uranium
- Mothers or fathers related
- Pesticides in drinking water
- Lead or arsenic in soil
- Heavy metals
- Polyethylene terephthalate (PET)
- Glyphosate
- Waste stream effluent
- Hazardous waste dumping as fertilizer
- Recreational drug use

DISCUSSION

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- What should be next steps in the investigation?
- What should be next steps for community outreach/prevention?

DEVELOPMENT OF ACTION PLAN

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