Anencephaly Investigation

Central Washington, 2010-2016

Advisory Committee Meeting
November 19, 2015

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PUBLIC HEALTH
ALWAYS WORKING FOR A SAFER AND HEALTHIER COMMUNITY

Surveillance Update

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

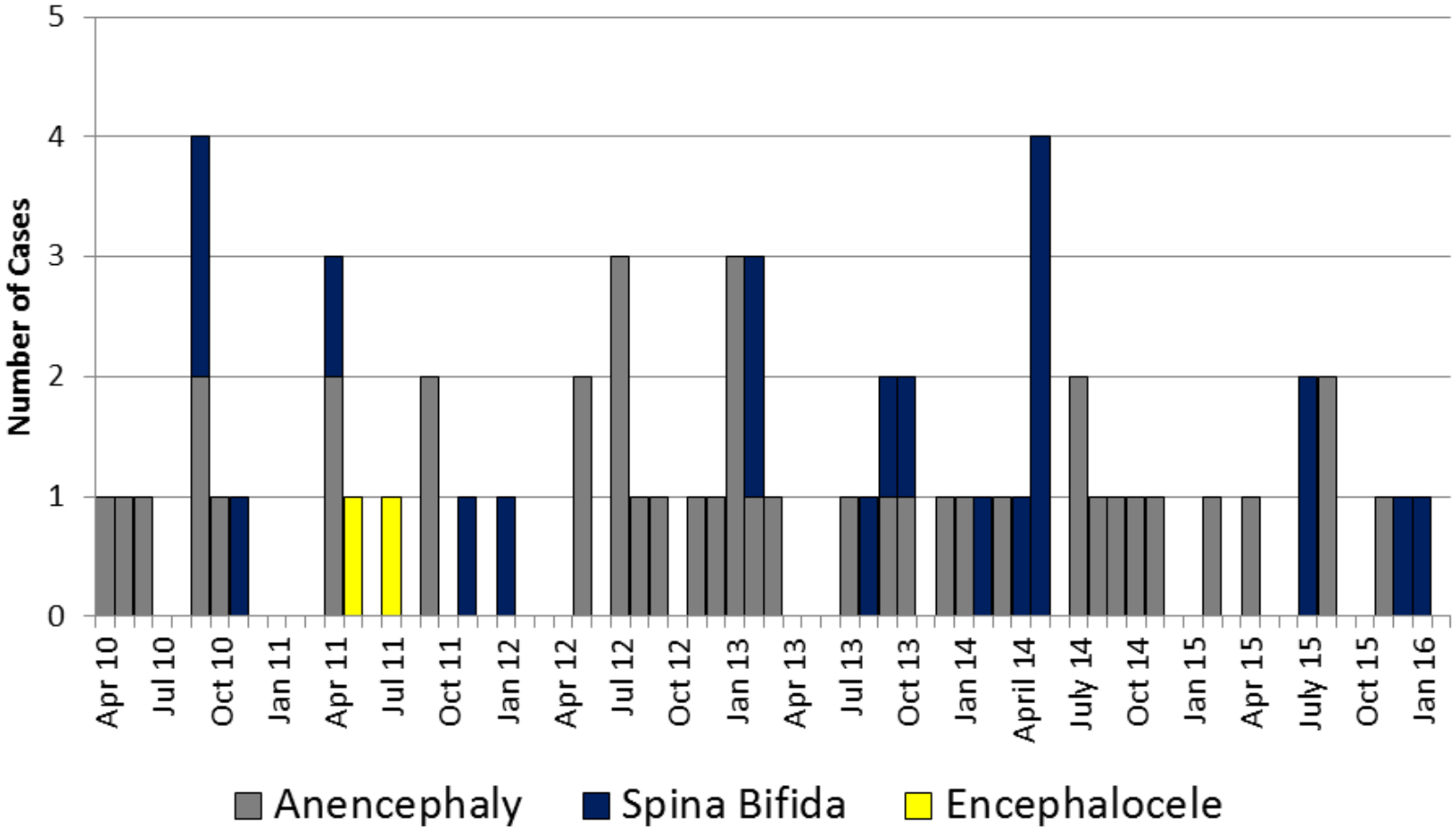
	Number	Total Births	Rate per 10,000 births	95% CI
All Neural Tube Defects				
2010	9	8565	10.5	(4.8, 19.9)
2011	8	8528	9.4	(4.0, 18.5)
2012	10	8352	12.0	(5.7, 22.0)
2013	14	8084	17.3	(9.5, 29.1)
2014	14	8432	16.6	(9.1, 27.9)
2015	8	NA		
2016	1	NA		
Total to date[2]	64	NA		

Anencephaly				
2010	6	8565	7.0	(2.6, 15.2)
2011	4	8528	4.7	(1.3, 12.0)
2012	9	8352	10.8	(4.9, 20.5)
2013	9	8084	11.1	(5.1, 21.1)
2014	8	8432	9.5	(4.1, 18.7)
2015	5	NA		
2016	0	NA		
Total to date[2]	41	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 October 10 with a delivery or estimated date of delivery in 2010-2016.

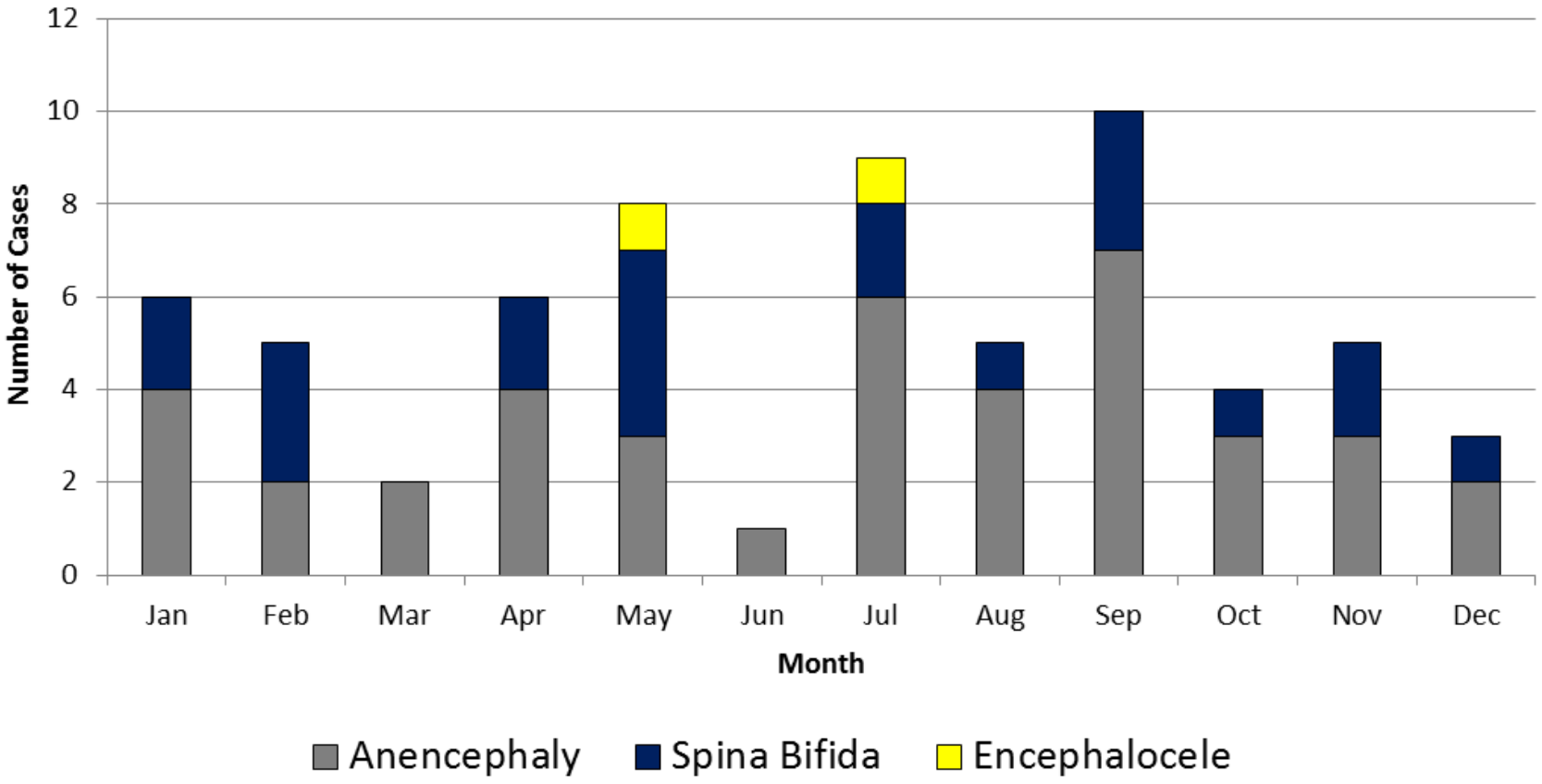
Neural Tube Defects by Month of Estimated Delivery Date[1]



[1]Estimated delivery date uses delivery date for gestational age ≥ 37 weeks and estimated delivery date for gestational age <37 weeks at delivery. Cases were confirmed through October 10, 2015.

Washington State Department of Health

Neural Tube Defects by Month of Estimated Delivery Date 2010-2016 Combined[1]



[1]Estimated delivery date uses delivery date for gestational age ≥ 37 weeks and estimated delivery date for gestational age <37 weeks at delivery. Cases were confirmed through October 10, 2015.

Washington State Department of Health

Washington Rates of Anencephaly and Spina Bifida[1]

	Anencephaly	Rate per 10,000	All Neural Tube Defects	Rate per 10,000	Births
2005	18	2.2	39	4.7	82,625
2006	13	1.5	45	5.2	86,845
2007	21	2.4	55	6.2	88,921
2008	24	2.7	59	6.5	90,270
2009	25	2.8	55	6.2	89,242
2010	27	3.1	53	6.1	86,480
2011	35	4.0	64	7.4	86,929
2012	23	2.6	49	5.6	87,417
2013	23	2.7	49	5.7	86,566
2014[2]	24	2.7	47	5.3	88,561
2015[2,3]	19	2.7	37	5.3	69,427
2005-2015	252	2.7	552	5.8	943,283

[1]Based on ascertainment from birth certificates, fetal death certificates and hospital discharge data, 2005-2013.
[2]Based on ascertainment from birth certificates and fetal death certificates only, 2014 and 2015.
[3]Limited to first 9 months of year using preliminary data file.

Interview Update

Interview Update

- 7 cases confirmed since spring (3 cases confirmed in April, 2 in August, 2 in October) have not been interviewed yet
  - Continue follow up with 5 mothers
  - 1 mother declined to be interviewed
  - Need to begin follow up with 1 mother
- Protocol sent to CDC
- Basic analysis planned due to small numbers
- Analysis of known NTD risk factors will be completed by spring, assuming CDC resource availability

Addressing Community Concerns: Nitrate

- N-nitroso compounds have been shown to be teratogenic in animal studies
- Drinking water nitrate levels associated with NTDs were relatively low
- Water – unless above the MCL – contributes only a small portion of dietary nitrate.
- Dietary nitrate has not been associated with NTDs
- Nitrate alone will not form N-nitroso compounds
- Nitrosatable drugs do show increased risks for NTDs in presence of nitrite in acidic environment.
- Many common drugs, including over the counter medications are nitrosatable drugs.

Addressing Community Concerns: Nitrate

- N-nitroso exposures come from a variety of exogenous and endogenous sources.
- Wouldn't expect a simple association between anencephaly or all NTDs and drinking water nitrates below the MCL alone.
- Nitrates in drinking water may be a proxy for another contaminant, but what?
- May be that a combination of dietary nitrate and drinking water nitrate contribute to increase risk, but this is difficult to tease apart even with several decades of research.

Addressing Community Concerns: Nitrate

- Investigation is looking for a common exposure related to NTDs that we could prevent.
- Nitrate in drinking water does not appear to be a clear risk factor for NTDs by itself
- Still, we took another look at drinking water nitrate levels among all 64 mothers of NTD-affected pregnancies
- Only have data from public water sources, although we did do some extrapolation to private sources based on surrounding public water source measures
- 80% of mothers were on public water supplies

Addressing Community Concerns: Nitrate

Public Water Supply only

	Min Nitrate Level	Max Nitrate Level	Average Nitrate
Anencephaly	0.05	9.26	1.91
Encephalocele	1.6	6.8	4.20
Spina bifida	0.05	5.5	1.54
Total	**0.05**	**9.26**	**1.89**

Nitrate level (mg/l)*	Anencephaly	Encephalocele	Spina bifida	Total
0	6		7	13
1	9		2	11
2	7	1	2	10
3	5		2	7
4	4			4
6			2	2
7		1		1
9	1			1
Total	**32**	**2**	**15**	**49**

Public Water & Extrapolated Private Systems

	Min Nitrate Level	Max Nitrate Level	Average Nitrate Level
Anencephaly	0.05	10	2.21
Encephalocele	1.6	6.8	4.20
Spina bifida	0.05	5.5	1.78
Total	**0.05**	**10**	**2.14**

Nitrate Level (mg/l)*	Anencephal	Encephaloce	Spina bifida	Total
0	7		7	14
1	9		3	12
2	7	1	3	11
3	5		2	7
4	6			6
5			1	1
6			2	2
7		1		1
9	1			1
10	1			1
Missing	5		3	8
Total	**41**	**2**	**21**	**64**

*Rounded to nearest whole number

Washington State Department of Health

Addressing Community Concerns: Pesticides

- Further explored 6 pesticides with positive associations from 2014 study in California.
- CA study found few associations among 461 chemicals and 62 groups explored. Associations may be due to chance.
- Looked at use of these compounds in Washington and potential for higher exposure in 3 county area compared to rest of state and elsewhere in the country.
- Looked at allowed pesticide use, and expected use in 3 county area based on professional judgment of WSDA experts, explored USGS maps of use across the country, reports of drift exposures, and whether any of the compounds had been identified in drinking water testing.

Addressing Community Concerns: Pesticides

- 6 pesticides: abamectin, 2,4-D, methomyl, imidacloprid, permethrin and bromoxynil octanoate.
- Chemistries of pesticides are all very different; other compounds with similar chemistries not found to increase risk.
- Use pattern: 5/6 pesticides expected to have higher use in other counties of state. Significant home uses for imidacloprid, permethrin, 2,4-D. Methomyl and bromoxynil are agricultural use only.
- WSDA record of drift cases does not suggest drift is common or occurring more in 3-county area.

Addressing Community Concerns: Pesticides

- Methomyl does have more use in 3-county area than elsewhere in state.
- Not found to cause NTDs in developmental and reproduction studies in rats.
- Major use in WA – potatoes, onions and wheat.
- Used seasonally, May-September in WA – no seasonal pattern of anencephaly.
- CA and FL have much higher use of this chemical than WA– so would expect to see increased rates in those states/areas if this were a causal association.

Addressing Community Concerns: Genetics

- NTDs are clearly associated with genetic factors, but it is not entirely clear what they may be
- Clinical concerns and concerns related to cause of NTDs
- Concerns about clinical care should be discussed with health care providers
- Etiologic inquiry could benefit from looking at cases with family history of NTDs and/or cases with multiple anomalies separately, but conclusions will be difficult

Addressing Community Concerns: Genetics

- NTDs associated with common polymorphisms in genes related to folate and homocysteine pathways
- MTHFR common genetic variant is 677C to T
- Having this variant associated with low tissue concentration of folate and increased homocysteine levels. Can be overcome with folate supplementation
- MTHFR polymorphism has population frequency estimated at 5-14 percent; most no NTDs
- Investigation focused on common exposures that could result in NTDs

Prevention Update

Prevention Update

- Vitamin Angels
  - Currently providing prenatal multivitamins in Yakima
  - Beginning mid-November will be providing prenatal multivitamins in Benton-Franklin

- Health Care Authority
  - clarifying policy for coverage of prenatal vitamins
  - will let the provider community know via written communication that daily multivitamin with folic acid (which contains the US Preventive Services Task Force recommended 400 to 800 mcg of folic acid) is covered for women of child-bearing age covered by Apple Health (Medicaid)

Prevention Update

- DOH Folic Acid: B Aware materials available for download and dissemination to clients:

  http://here.doh.wa.gov/materials/folic-acid-b-aware

- Folic acid fortification corn masa flour
  - Stability study being conducted is complete
  - Findings have been presented to FDA
  - Awaiting decision from FDA

References

Brender JD . Nitrate, Nitrite and Nitrosatable Drugs, and Congenital Malformations. In: Watson RR, editor.. Handbook of Fertility. London: Elsevier; 2015. p 61-74.

Yang W, Carmichael S, Roberts EM, Kegley SE, Padula AM, English PB, Shaw GM. Residential agricultural pesticide exposures and risk of neural tube defects and orofacial clefts among offspring in the San Joaquin Valley of California. Am J Epidemiol 2014; 179:740-748

Questions/Comments?

To provide comments or questions, please contact:

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