

Anencephaly Advisory Committee Meeting (webinar)
Minutes
August 23, 2016

Advisory Committee Members present:

Kathy Lofy, MD, Chair
Susie Ball, MS
Sara Barron, RN
Lisa Galbraith, MD
Peter Langlois, PhD
Gina Legaz, MPH
Christina Nyirati, PhD, FNP-BC
Amy Person, MD
Melissa Schiff, MD, MPH
Vickie Ybarra, PhD, MPH, BSN

WA Dept of Health Staff present:

Zachary Holmquist, MPH
Katie Meehan
Paj Nandi, MPH
Cathy Wasserman, PhD, MPH

Interested parties were sent information about the meeting and asked if they wanted to participate. There were several interested parties on the call, including representatives from the media.

I. Welcome and Introductions

Kathy Lofy began the meeting at 8:05 am.

Cathy Wasserman gave a presentation updating advisory committee members on the status of surveillance, investigation and prevention efforts (attached). The presentation included new numbers of cases confirmed since May 6, 2016 and the following highlights:

Surveillance Update:

- Two new neural tube defect (NTD) cases have been confirmed. One new anencephaly case due in 2017, and one case of spina bifida due in 2016. Latest numbers also reflect the one spina bifida case from 2015 whose mother did not reside in Washington until just before delivery.
- Total number of NTD cases in the three-county area is 69 confirmed since 2010, including 44 cases of anencephaly. Current numbers reflect cases confirmed through July 15, 2016.
- Slide 4 was presented in May and compares anencephaly rates using different inclusion criteria to rates reported to the National Birth Defects Prevention Network (NBDPN) from states for 2007-2011. The Washington dates overlap with these dates, but are not exactly the same time frame. The graph on slide 4 shows the variability in reported rates across states. The blue dots reflect registries that include all live births, terminations and stillbirths. Some states have active ascertainment and some have passive ascertainment. The orange dots reflect registries that include live births and stillbirths only, and the green dots include live births only. The graph shows a lot of variation from state to state which is not well understood and could be due to true differences, a difference in surveillance methodology – or a combination of the two. Washington rates are higher than what has been reported by most other states, but depending on the definition, closer to the range of reported rates than our assessment of a four-fold increase.

- We noted that almost half (49%) of the anencephaly cases in the three-county area were among pregnancies that ended before 20 weeks gestation. This is very early in pregnancy and these cases may not be seen at hospitals where many registries identify NTD cases. We contacted Texas and California to explore whether a similar proportion of anencephaly cases were identified and terminated early in pregnancy. Slide 5 shows the results of our inquiry, on the left hand side for all cases compared to Texas, and on the right hand side for Hispanic cases only compared to California. While almost half of our cases are from those that ended prior to 20 weeks gestation, less than a quarter of the Texas cases are from this group. Among Hispanic only cases, about 41% of our cases were from the early time period compared to about one-third of the California cases. Given the relatively small number of cases, these differences may not be statistically significant, but they suggest that we may be ascertaining cases earlier than in other locations, and possibly capturing cases that are missed by other registries.
- Slide 6 looks at the proximity to production agriculture using the Washington State Department of Agriculture's crop maps. This exploration considers proximity to agriculture as a proxy for pesticide exposures. The table at the top has rows for anencephaly cases, spina bifida combined with encephalocele cases, and a row for controls. For the controls, we used all live births and fetal deaths in the three-county area from 2010-2014. Distances are calculated as the distance to the closest field in agricultural production. Below the table is a box plot. This shows pictorially the same information as the table. The dark line in the middle of each box is the median. Half of the cases are closer than this level, and half farther away. On average, the controls live closer to production agriculture than do anencephalic cases, but all three groups are very similar.
- On slide 7, we were interested to see if we could determine the parental occupations of all identified cases. Birth certificates and fetal death certificates capture the reported occupation of mothers and fathers. We only had certificate information for 43 cases, with 37 having occupation reported. This table shows all occupations that were reported for more than one case mother or father. There was no job among which case mothers or case fathers stood out.
- In summary: cases have occurred across all years with no strongly defined peaks in time. There is no strong seasonality. There is continued predominance of anencephaly over all other NTDs. Our rates from the three-county area appear on the high end of state rates across the country, but the increase is likely not as extreme as we originally thought. We are ascertaining more cases in the three-county area earlier than in Texas or California, so we may be doing a better job of case ascertainment. Cases and controls live the same distance from production agriculture and no occupations stand out as more frequent among case mothers or fathers.

Investigation Update:

- We have continued to follow up with women, attempting to interview new cases.
- Slide 10 summarizes the interview findings of cases confirmed by October 10, 2015. We have additional interview information which we will add when we have five completed interviews of a given case type.
- Compared to all case mothers, interviewed mothers are similar age, fewer Hispanic/Latina, and more have had a prior pregnancy.
- Compared to all birth mothers, interviewed mothers are older, fewer Hispanic/Latina, similar proportion born in Mexico, have a higher educational level, and are more likely to have had a prior pregnancy.
- All 17 interviewed case mothers used prenatal vitamins at some point in pregnancy, and eight or 75% of anencephalic moms used prenatal vitamins during the critical window. This is more than our estimates based on Pregnancy Risk Assessment Monitoring System (PRAMS) data and initial case-control study.

- Seventy-five percent of mothers of anencephalics worked during the critical time period for NTD formation, and four (33%) were assessed as having probable pesticide exposure based on their reported jobs, mostly but not all due to farm-related jobs.
- We plan to compare data from interviewed case mothers in Washington to interviewed control mothers from California and Texas who participated in the NBDPS from 2004-2011. We will compare known risk factors for NTDs: family history, diabetes, Hispanic ethnicity, obesity and the use of folate antagonists. We will also explore parental occupational pesticide exposures.

Prevention Efforts Update:

- In May/June, we did some intercept interviews in Benton, Franklin, and Yakima counties to determine how we could improve our outreach and messaging. We got some help from students at Central Washington University, and went to several locations to identify women of reproductive age. The results are not generalizable to the state as a whole, but they provide us with useful information that can help us plan our prevention messaging going forward.
- Slide 15 shows demographics of women contacted.
- We looked at results of where women preferred to get health information by ethnicity and the preferences were more or less the same. The top preference for Latina and non-Latina women was to receive information from their health care provider or clinic. After that, Latinas preferred to learn about health information online and then from family or friends, while this order was reversed for non-Latina women.
- We showed participants a list and asked who they would prefer to receive health messaging from. Women identified their primary care provider or OBGYN as the most trusted health care professionals. This information is helpful for planning outreach strategies.
- About half of interviewees established that they had not heard about folic acid prior to pregnancy, and that they wished they had received more information. Sixty percent stated that they started prenatal vitamin use once they found out they were pregnant.
- Almost 80% reported that they will definitely ask their provider for a prescription for prenatal vitamins if their insurance covers them. Unfortunately, not a single interviewee with Apple Health (Washington's Medicaid program) knew about the new coverage that is available for prenatal vitamins.
- We also asked about motivating factors for taking vitamins, and learned that women were motivated because they thought: 1) it was good for their own health, 2) it was good for the baby's health, and 3) they were told by doctor or midwife that it was important to take a prenatal vitamin. Women talked about not getting enough education ahead of time, and when they did learn about folic acid they were mostly just told to take it, rather than explaining why or what the benefits were. We also asked about the top barriers to taking prenatal vitamins that they experienced, or things they heard from friends and family. Women reported that they had heard vitamins make you sick, they didn't really know why they were important, or that they simply forgot to take them.
- We also asked about their knowledge of NTDs and anencephaly. Seventy percent of women had never heard of anencephaly or NTDs, and only approximately half of participants wanted to have more information about anencephaly prior to pregnancy. The interviewees were typically more concerned with the birth defects that they were already aware of, like Down syndrome and cleft palate.
- These interviews resulted in three recommendations for future outreach: incorporating folic acid education into medical appointments, using social media to raise awareness, and sharing important health updates through local media. Women's health exams, or when they get their birth control refills, seem to be the most opportune times to educate these women. Because the women we talked to used social media as a way to access information, we think the use of social media ads to raise awareness about folic acid could be a good channel to get that message out. In June, we piloted some folic acid messaging on social media. The ads outperformed industry standards so we feel this is

a good channel for us to continue to explore. We also want to target messaging locally, because women also appear to be paying attention to their local media.

Investigation Conclusions:

- We met with local health jurisdiction staff over the summer to review the findings to date and discuss future efforts. Together, we offer the following conclusions;
 - o We believe that the elevated rate of anencephaly is due in part to more complete ascertainment of cases in the three-county area.
 - o Because cases are not strongly clustered in time or space, it is more challenging to identify a preventable cause from the multiple factors that lead to NTD cases, and neither our case-control analyses of medical records nor our interviews with mothers of cases have identified an actionable, preventable cause.
 - o Despite pursuing a number of hypotheses, there is still no evidence that the elevated rate is due to folic acid deficiency, nitrates in the local drinking water, pesticide exposure, or radiation from the Hanford site -- some of the community's greatest concerns.
 - o We have not identified prevention opportunities beyond promoting preconception folic acid supplementation; and
 - o Given these conclusions, we feel resources should be focused on outreach to educate women about prevention and early detection of NTDs, as well as the promotion of preconception and pregnancy health.

Recommendations for Future Activities

- We recommend completing the comparison of case-control data using the NBDPS controls from Texas and California. If no hypotheses are identified, we recommend ending the investigation component of our response, and incorporating all of the findings into a report. We are currently working on drafting a report, and barring any changes would plan to share a draft of the report with the advisory committee for feedback this fall.
- We recommend continuing stimulated passive surveillance with area hospitals and providers through next August, reviewing the findings at that time and making further decisions about surveillance then as well.
- We recommend incorporating the lessons learned from our intercept interviews into our continued outreach, as well as the development of preconception and pregnancy materials, and our department efforts to improve access; and
- Lastly, we suggest continued work in collaboration with local health jurisdictions and other partners on folic acid outreach, communication and improvement of preconception and pregnancy health.

Advisory Committee Questions and Comments

Advisory Committee (AC): In the intercept interviews did the women indicate what the reputable news sources were that they used when they looked at social media?

Department of Health (DOH): We did ask that and for the most part people were unable to remember the name of the channel. For local news channels we would ask what they were and people could not remember the name most of the time, usually just remembering that it started with a K or something. In terms of social media it was anything that was trending that was from a news source. When you log into Facebook, on the right side you see the stories and articles that are trending.

AC: So major news sources?

DOH: I think local channels or newspapers would be good outlets for us to look into.

AC: Thank you.

AC: I had a question about the case-control interviews, could you talk about the response rate?

DOH: We found and continue to find that we are often able to locate the women and that they agree to participate, but when we call to set up an interview we have a difficult time setting up the interview itself. In some instances it looks like mothers were ill and could not participate. In other instances we just are not able to get anyone to pick up the phone. Does that answer your question?

AC: Yes

AC: I wonder if we have any information about corn masa products being distributed in Washington. Do we know if they now contain the voluntary folic acid fortification?

DOH: When they were initially approved, we heard that they would be on the local market quickly but we can look into that. Gina is on the line and may have some additional information?

AC: I do not, sorry.

DOH: I will get some more information on whether they have made their way to the local market and get back to you.

AC: Thank you.

DOH: If there are no additional questions on the line, I would like to spend some time looking at the proposed future activities and get some feedback on the direction we are headed.

AC: I was at the meeting this summer, and I think what is proposed seems reasonable, and the direction you outlined seems good.

DOH: We would love to hear from others, too. I am not sure how to interpret the silence.

AC: I concur. I think the direction that the data gathering has taken is wonderful. I think that the data are excellent, and that there should be work with regular health care providers so they are more communicative with women or reproductive age about using folic acid regularly since the data show that women were naïve to the use of preconception use of folic acid.

DOH: Thank you, we agree. For those of you who might not know, the Washington State Hospital Association is undertaking a QI project about preconception, pregnancy, labor and delivery, and post-conception, and of course folic acid is a part of that. They are working hard to get providers to use these 'bundles' of best practices.

AC: I concur, and I think the proposed activities are worth supporting. I would like to see a formal communication plan as outlined in that last bullet, and I would like to see fortification included in that communication plan. I do not think many women in our target population are aware of it and how they get it in their diet. Besides that I do support the efforts outlined.

DOH: Just to follow up on that, we do have Katie and Paj who have worked on the outreach piece. We do have an outreach plan that we need to revisit now that we have this additional information from the local women.

AC: I agree with the plan as well, and my one comment was going to be continued surveillance, but it looks like you will be reevaluating that again next year anyway so it will come up for conversation.

AC: I would hope that going forward you can look at the whole state by the regions that you had at the last meeting. I was worried that central Washington had rates of 4.5 versus King County which has 1.5. Do you have any comments on that?

DOH: Yes, Remember the statewide data are based on different ascertainment, and we do not know if the differences there are true differences, or are due to demographics or a different decision making process after a diagnosis of anencephaly or NTD. Just within the three-county area when I looked at (and I did not show this data), the early diagnosis and termination versus live born or fetal death cases and stratified by race/ethnicity, we have a lot more non-Hispanic white women who are terminating anencephaly prior to 20 weeks gestation as a proportion of all cases. It was 49% overall, and something like 70% for non-Hispanic whites.

AC: Has there been further analysis to determine the contribution of prenatal diagnosis [of an NTD] and termination to the reduced or the lessened rates in King County in comparison to the higher prevalence in women who have early prenatal diagnosis and do not terminate?

DOH: We do not really have a data source to look at that.

DOH: We can look at live births and deaths greater than 20 weeks.

DOH: We would miss those women who are diagnosed early and are not terminating in the hospital.

AC: There is no way to track women who abort early in pregnancy using vital records?

DOH: No, not using vital records.

DOH: It is widely accepted that there are differences in decision making after a diagnosis rather than letting the pregnancy go to term. I am seeing also that Sara Barron has written in that Okanogan has a high rate also, not just the three-county area. Generally eastern Washington has higher rates based on ascertainment from vital statistics data only.

AC: What about rates of prenatal care access?

DOH: We have general information on when women start prenatal care.

DOH: Are you suggesting that cases in western Washington are detected earlier?

AC: I am asking that question, if we can look at that overall.

DOH: We can look at prenatal care overall, we do know that in Benton and Franklin counties historically they have higher rates of initiating care later. Amy might have something to say here, as they have tried to encourage providers to see women earlier in pregnancy.

DOH: Lisa can maybe say if the OBGYN practices are different in the three-county area than in any other part of the state.

AC: We have improved our percentage as far as not seeing so many women foregoing prenatal care, but I do not know if we have crossed a threshold with early diagnosis. We might see women a little later than average, but I do not have any data on that.

AC: I am sure you have differences by race/ethnicity in the week they begin prenatal care and the rates of anencephaly before 22 weeks by ultrasound, and testing of the alpha fetoprotein before the 22 week of pregnancy. But if a woman does not begin care before the 22nd week of pregnancy, the likelihood of having a termination – the research is conclusive that women from every ethnic and cultural group, racial group are reluctant to have a termination after 22 weeks regardless of personal beliefs or ethnic/family beliefs. If women do not begin prenatal care until 20 or 22 weeks, the likelihood that they would elect to end a pregnancy is much less than a woman who initiates prenatal care in the first trimester and has an alpha fetoprotein test before the 17th week.

DOH: I can pull together the information statewide and by county on prenatal care initiation, whether it is the first trimester, the second trimester or later. I do not know off the top of my head, my sense is that if women are not getting in during the first trimester mostly they are getting in by the early second trimester. We do not know what the content of their visit is, but we can see when they are getting prenatal care and look at it by race/ethnicity and county and provide that to you all. In the three-county area, we are seeing more women who are diagnosed and terminating early in comparison to some of the other active registries in Texas and California. It is kind of the opposite point, that we are getting more women who are diagnosed and terminating early rather than fewer women.

DOH: We are at the top of the hour and I want to respect your time. As Cathy presented, we are going to finish the comparison of the case data to the control data, and if there is no hypothesis that is identified we will have to alter our response. It is possible that the meeting we have in November may be the last advisory committee meeting, and some of you have asked how long this will go on for. We want to thank you for the time you have committed to these meetings, and we really do appreciate the time and effort that you have committed to participate in the effort overall. I just wanted to take a look and see if there are questions from members of the public. We will stay here for a few extra minutes to answer questions from the public.

Public: Have you looked at the study “Prenatal Nitrate Intake from Drinking Water and Selected Birth Defects in Offspring of Participants”? It is from the NBDPS. This study was actually in Iowa and Texas. The study found that drinking nitrate levels greater than 5 parts per billion (5 ppb) doubled the risk of spina bifida. I am doing water testing in the Yakima Valley area, and I have found that a lot of the water is higher than five. Have you looked between 5 and 10?

DOH: Yes, we presented the results of those findings this winter. If you can provide me with your email I will provide you a reference to a chapter written by Jean Brender. She authored a chapter in which she goes over the literature in depth. We have had conversations with her, and I am happy to share the reference. We cannot share the paper directly because of copyright issues, unfortunately, but I can send the reference and you can look for it.

Public: The study I am citing is one of her studies, and it looks like the rate of NTDs increased significantly between 5 and 10 ppm for nitrates.

DOH: These are not experimental conditions, so we cannot base conclusions on a single study. What we generally do is study the literature, the entire body of studies, and make conclusions using that. Dr. Brender has spent her career looking at nitrates in water and birth defects. I can send you a recent chapter she wrote summarizing nitrates, nitrites and birth defects, and how nitrates react with nitrites and nitrosatable drugs. I am happy to share that information with you.

Public: I would like to see it because that is the opposite of the findings that this study presented. We do have a lot of small towns where the initial level will be above 10 and it will be diluted down to 9, and I am seeing a lot of houses in the 6 or 7 range.

DOH: We have your email, and I will forward that to you after the end of this call.

Media: Hello this is JoNel with the Seattle Times. It sounds like you are saying we are doing better ascertainment than Texas and California, and the problem may not be as severe as we thought because of that better ascertainment. If we do not think the rate is as extreme as we thought, do we have an idea why that might be the case?

DOH: In the slide where I show the variation across the states, you can see that there is significant variation in rates. It is not like these states all have a rate that is 2 per 10,000. You can see that the rates across states vary tremendously.

Media: Sure. So when we are communicating this to the public, because we started with the initial study in 2012, should we say that we are continuing to have cases, but the problem does not appear to be as extreme or severe as public health officials initially thought?

DOH: I think we can say that after digging a little deeper, we have learned there is a lot of geographic variability across areas and we do not know why that exists.

Media: Okay, thank you so much,

Public: A local physician recently brought to my attention some journal articles that link elevated nitrate with elevated uranium in the drinking water, and then related to me articles showing that increased uranium can lead to multiple types of defects, one being NTDs. Do we know if anywhere in the Yakima valley, do we have any evidence about what we may have been experiencing in terms of uranium exposure?

DOH: I would have to check with our drinking water people, could you email me those journal articles?

Public: Sure.

DOH: Thank you for joining, and sorry that we ran over a little bit. We wanted to be sure we could answer questions for the public. We will talk to you again in November, good bye.

Meeting Ended at 9:13 am.