



Clinical and research commentary on recent Danish alcohol in early pregnancy research

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The headline reads, ***Moderate drinking in early pregnancy branded 'safe'***¹. This was prompted by Danish research published last week in the British Journal of Obstetrics and Gynaecology² which failed to find any significant neurodevelopmental deficits in 5 year olds who had been exposed to low and moderate amount of alcohol during early pregnancy.

However, responses from other experts sound a warning about accepting such interpretation at face value. Alcohol is a known teratogenic agent that is toxic to fetal development during gestation and no safe threshold of exposure has yet been found. To their credit the researchers also concluded that safe levels of alcohol use during pregnancy had not been established. However this was not their primary emphasis.

Many commentators express concern about studies like these sending mixed messages to women and may lead to a false sense of security. Professor Jennie Connor, head of the Preventive and Social Medicine department at the Dunedin School of Medicine, said there was a risk the Danish studies could lead women to believe it was reasonable to drink during pregnancy as long as it was not too much. So what should women know about alcohol and pregnancy and where does the truth lie in regards to the research?

The researchers studied 870 preschool children whose mothers reported drinking during pregnancy and compared them to 758 preschool children whose mothers reported not drinking during pregnancy. Overall, the researchers found that low to moderate weekly drinking in early pregnancy had no significant effect on neurodevelopment of children aged five years, nor did occasional binge drinking. They did however, find a positive association between a lower attention span among the five-year-olds at an intake of nine or more standard drinks per week.

Associate Professor Kathryn Kitson, from Massey University's Institute of Food, Nutrition and Human Health, wanted media reports to emphasize that as few as nine drinks a week showed association with an increased risk of attention problems in children. Dr Kitson points out that a cautious safety recommendation would be at a 1000-fold or less below the level of indicated

¹ <http://www.bbc.co.uk/news/health-18506174>

² <http://www.bjog.org/view/0/searchResults.html?q=kesmodel>

damage from a toxin. *"On that basis a 'safe' limit for alcohol during pregnancy should be around 0.009 drinks a week, essentially no alcohol at all. Alcohol alters fetal development by interfering with intricate mechanisms that regulate switching genes on and off at critical development stages", she says.*

So what of the actual research?

The Danish researchers looked at the IQ, attention span, executive functions and self-control in five-year-olds who had been exposed to alcohol by their mothers in the first half of pregnancy. This was later co-related to the levels of drinking reported by the mothers at the time of pregnancy.

According to experts who assess children with Fetal Alcohol Spectrum Disorders, the big issues around the Danish research are the age of the children in the study, the use of parental reporting and how they have categorise alcohol consumption and some questions that remain around some of the research statistical analysis.

As one New Zealand expert Andi Crawford, a Clinical Psychologist who specialises in assessing children for FASD notes, 69 percent of the sample 'binge drank' once in their pregnancy which was then surmised in one of only two categories - 'Any' binge drinking or 'No' binge drinking. *"Extrapolating their data to say there is no effect of binge drinking and children's cognition is a large leap as most of the women in this study consumed alcohol at this level only once. Moderate drinking of 5-8 drinks per week appears equally misleading, It is not clear whether this was for just one week or many weeks".*

Measuring executive functioning in 5 year olds is problematic and this was acknowledged in the research, However Ms Crawford points out that even their measures of cognition are problematic. *"VIQ is measured by 3 subtests - arithmetic, information and vocabulary. Information and Vocabulary are learnt functions and we know that children with FASD or prenatal alcohol exposure are more able to perform well in tasks they can learn by rote and repetition. Arithmetic involves a more complex working memory function but at age five tasks are relatively simple. Furthermore I couldn't find if there were more specific correlations with alcohol than just the arithmetic subtest".*

Measuring attention tasks may not show the complexity of attention issues. The attention tasks for Selective and Sustained attention were also relatively straight forward. *"We find that often children with FASD can perform simple tests of attention such as visual scanning and processing simple routine information but their ability to sustain attention decreases when the task becomes more complex. In addition we find that children with ADHD and or FASD have many sensory processing problems so therefore attention tests performed in a one-on-one quiet environment do not always show the attention difficulties children have in a busy classroom."*

Missing values in the TEACH assessment tool used to measure attention may also have skewed the data. There were 249 missing values for the TEACH due to issues such as motivation, not

understanding the task, and lacking the ability to perform. *“They used ‘multiple imputations which yields unbiased estimates if data is missing...based on predicative distributions for missing values’. My understanding would be that the children who were missing the data were probably the ones with attention impairments. I have often found that low motivation is linked to a child’s low confidence/ability in being able to complete the task. In addition, children with Prenatal Alcohol Exposure can have attention problems which are more than we can expect from IQ. The researchers also said that the BRIEF instrument had a low correlation with attention tasks. On that basis, neither of these measures would be good to estimate the missing values on a group of children who were likely to have more severe attention problems. We know that parent report is more subjective than standardised tests. Andi Crawford hoped that the researchers addressed some of these issues and continued with assessing children when they are at least 8 years old.*

Dr Therese Grant and Dr Susan Astley of the University of Washington³, say the reason the children in this study did not appear to be harmed by the alcohol is because the children were too young to measure the full impact alcohol may have had on their brains.

“At 5 years of age, the brain is still developing. A 5-year-old’s brain is not developed enough to perform complex tasks like remembering and following multiple instructions, writing an essay, communicating abstract ideas effectively, exercising good judgment. Over 30 years of research on fetal alcohol syndrome (FAS) confirms that alcohol has its greatest impact on complex brain functions. This is why children exposed to and damaged by prenatal alcohol exposure look deceptively good in the preschool years. The full impact of their alcohol exposure will not be evident until their adolescent years, they say.”

These experts cite statistics that are based on 2,600 children who received a diagnostic evaluation for FAS in the Washington State FAS Diagnostic & Prevention Network clinics over the past 18 years and compare this with the Danish data as follows:

The Washington data indicates that 1 out of every 7 children diagnosed with FAS (the most severe outcome caused by prenatal alcohol exposure) had a reported exposure of 1-8 drinks per week. (The Danish study did not conduct FAS diagnostic evaluations on the children).

Half of the children with FAS had developmental scores in the normal range as preschoolers. But all had severe brain dysfunction confirmed by age 10. (The Danish study only assessed preschoolers). Only 10percent of the children with FAS had attention problems by age 5. 60percent had attention problems by the age of 10. (The Danish study only assessed attention at age 5).

³ Susan Astley Ph.D. is a professor of Epidemiology and Pediatrics and director of the WA State FAS Diagnostic & Prevention Network of clinics (fasdnp.org). Therese Grant Ph.D. is director of the Fetal Alcohol and Drug Unit in the Dept. of Psychiatry & Behavioral Sciences (<http://depts.washington.edu/fadu/>). Both are research affiliates at the Center on Human Development & Disability at the University of Washington.

Only 30percent of the children with FAS have an IQ below normal. But 100percent had severe dysfunction in other areas like language, memory and activity level (The Danish study did not assess these areas).

And so these and other specialists conclude that, while the science may be complicated and studies sometimes yield conflicting messages, the message for women is simple: to have the *healthiest baby possible*, don't drink alcohol when you're trying to get pregnant and during pregnancy.

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