

How much alcohol can a  
woman drink during  
pregnancy and be sure to not  
harm her baby?

Why the answer is none.

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# Disclosure Declarations

Name	Disclosure
Sandra J. Kelly, Ph.D.(Instructor)	Nothing to disclose
Kerry Mauger, (Planner)	Nothing to disclose
Karen Wolf-Branigin, (Manager)	Nothing to disclose
Leigh Ann Davis, (Manager)	Nothing to disclose

# Outline

- A. Historical Overview
- B. Blood Alcohol Levels
- C. Alcohol and Genetics
- D. Alcohol and Other Factors
- E. Summary

# A. Historical Perspective on FASD

- Alcohol as a drug probably produced millions of years from fermented fruit

- Earliest concrete evidence comes from wine in Neolithic times, 10,000 years ago; also 9000 years ago wine from rice & honey in China
- Code of Hammurabi in 2225 BCE, Egyptian Book of the Dead from 3000 BCE



- References to alcohol's effect on the child of a woman who drinks alcohol during pregnancy in the Judeo-Christian Bible, ancient Greek and Roman times
- General belief of moral failing being passed on by the alcoholic mother in 1800's, early 1900's



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# A. Historical Perspective on FASD

- Early research on FASD
  - Sullivan, W.C. (1899). A note on the influence of maternal inebriety on the offspring. *Journal of Mental Science*, 45, 489-503.
  - Lemoine, P., Harousseau, H., Borteyru, J.B., & Menuet, J.C. (1968). Les enfants de parents alcooliques. Anomalies observées, à propos de 127 cas. *Quest Medical*, 21, 476-482.
  - Jones, K.L., Smith, D.W., Ulleland, C.N., Streissguth, A.P. (1973). Pattern of malformation in offspring of chronic alcoholic mothers. *Lancet*, 1, 1267-1271.
- 1970's: Studies on FASD and animal models of FASD focusing on proving that alcohol was the culprit (a teratogen)



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# A. Historical Perspective on FASD

- 1981 Surgeon General Report warning against drinking while pregnant
- 1980's and 1990's research focused on describing the effects of alcohol on the individual or animal
  - Which brain regions were particularly vulnerable
  - Pattern and timing of alcohol and damage
- 2000's to present: Relating specific brain regions to behavioral deficits and focus on treatment (not a cure) and prevention

# A. Historical Perspective on FASD

- **Characteristics of Fetal Alcohol Syndrome (Jones and Smith, 1973)**
- **Fetal Alcohol Spectrum Disorders**
- **Prevalence**



Wattendorf et al., 2005

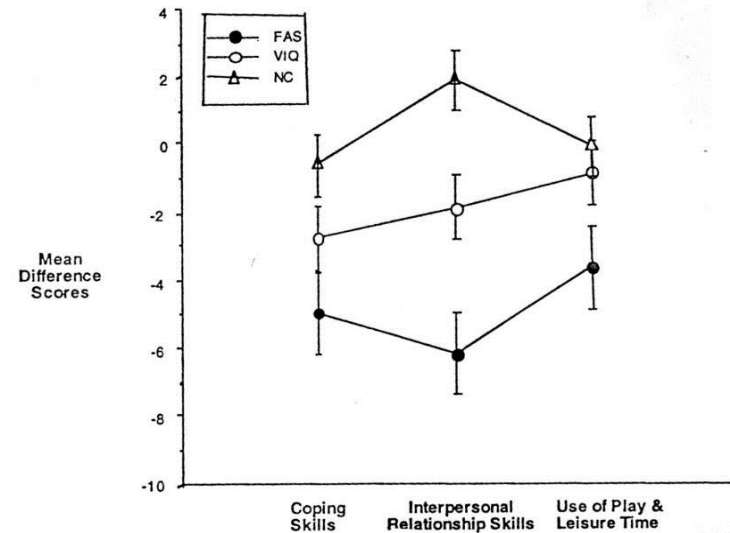
# A. Historical Perspective on FASD

- **CDC:**
  - **Fetal Alcohol Syndrome:** Abnormal facial features, growth problems, Central Nervous system Defects (Structural, neurological, functional (either cognitive deficits generally or specifically in executive functioning, social skills, attention problems), Alcohol use during pregnancy (optional)
  - **Alcohol-related Neurodevelopmental Disorder (ARND):** functional effects
  - **Alcohol-related Birth Defects:** Organ systems other than brain
- **Neurodevelopmental Disorder associated with Prenatal Alcohol Exposure (ND/PAE) **DSM 5:315.8****



# A. Historical Perspective on FASD

- FASD is not simply cognitive dysfunction and seems to have a unique distribution of symptoms, particularly in the social domain.
- Mysterious maladaptation and problems in executive function (Clarren, 2014 webinar)
- Generalized deficit concept (Quattlebaum and O'Connor, 2013)



Thomas, Kelly, Mattson, and Riley, 1998)

# A. Historical Perspective on FASD

- Secondary Disabilities (CDC Final Report, 1996)
  - Mental health problems particularly attention deficit, depression, anxiety (90%)
  - Disrupted school experience (40%)
  - Trouble with the law (40%)
  - Confinement (32%)
  - Inappropriate sexual behavior (43%)
  - Alcohol and drug problems (20%)
  - Dependent living 21 years and older (82%)
  - Problems with employment 21 years and older (79%)

# A. Historical Perspective on FASD

- How much alcohol is harmful to the developing fetus?
- How much can a woman drink while pregnant and be sure her baby is safe?
- The answer is none and here is why - -

# B. Blood Alcohol Levels

- Alcohol as a chemical
  - Simple chemical causing diffuse effects in the brain and other tissue
  - Crosses brain and placental barriers easily
    - Blood alcohol levels are the same in mother and fetus
  - Toxicity effects on tissue including brain both in adults and in the fetus

# B. Blood Alcohol Levels

- The amount of alcohol total is not the key; it is the blood alcohol level that is predictive of damage to the developing fetus.
- Determinants of Blood Alcohol Level
  - How much alcohol
  - How quickly the alcohol is ingested
  - The presence of food in the stomach and intestines
  - Size of the individual, body fat composition
  - Liver status and alcohol metabolism



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# B. Blood Alcohol Levels

- Timing of Alcohol Exposure
  - May et al., 2013
    - Bingeing particularly predicts FASD and poor outcomes especially low non-verbal IQ, poor attention, and behavioral problems
    - First trimester drinking elevates risk for FASD 12 times
    - Drinking beyond the first trimester elevates risk for FASD over 60 times
  - Brain is particularly impacted by drinking alcohol during third trimester.
- Impact of low amounts of alcohol
  - In animal models, detection of learning deficits and brain changes in offspring with blood alcohol levels around 70 mg/dl (or 0.07) in the dam have routinely been shown.
    - People can get to blood alcohol levels of 0.07 with two drinks depending on factors influencing metabolism.



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# B. Blood Alcohol Levels

- **So what does this mean for the pregnant woman?**
  - A pregnant woman and her fetus will be exposed to the same level of alcohol concentrations.
  - Low levels of blood alcohol concentrations can damage the fetus.
  - The degree of damage to the fetus is a function of timing during pregnancy.
  - How much alcohol gets into the blood depends upon the way in which alcohol is ingested, when it is ingested and the individuals' ability to metabolize alcohol (liver, body size, etc.).

# C. Alcohol and Genetics

- Even with blood alcohol levels held constant, the genetics of an individual determines alcohol's impact on brain and other organ systems
- Observations of twins exposed to alcohol *in utero*
  - Identical vs. Fraternal Twins (Christoffel and Salafsky, 1975)
  - Streissguth and Dehaene (1993)
    - Concordance in diagnosis of FAS for all identical twin pairs but discordant diagnosis for 7 of 11 fraternal twins



**Genetics or Placental Differences?**  
**Answer from animal models of FASD**



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# C. Alcohol and Genetics

Paternal Maternal	B6	SS
	B6B6 (61%)	B6SS (28%)
B6		
SS	SSB6 (3%)	SSSS (16%)

.....

Gilliam et al,  
1997

Crosses between Different Strains of Mice (B6 and SS) which are genetically identical

Impact of fetal and maternal genome on malformations induced by exposure to a high dose of alcohol given once during pregnancy



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# C. Alcohol and Genetics

		B6 Transferred		D2 Transferred		B6 Natural			D2 Natural	
		Maltose	Ethanol	Maltose	Ethanol	Unexposed	Maltose	Ethanol	Maltose	Ethanol
B6 Dam	Digit	0/6	9/18	NA	0/10	0/25	0/42	20/69	0/11	0/16
	Kidney	0/1	1/5	NA	1/4	0/13	2/24	9/38	1/5	2/9
	Vertebral	0/5	2/13	NA	4/6	0/12	0/28	7/31	1/6	0/7
	ANY	0/6	9/18		5/10	0/25	2/42	30/69	2/11	2/16
D2 Dam	Digit	0/7	10/33	0/6	0/4					
	Kidney	0/3	5/15	0/3	1/1					
	Vertebral	0/4	5/18	0/3	0/3					
	ANY	0/7	16/33	0/6	1/4					

Gilliam, 2014

Table numbers represent number of fetuses with a malformation (numerator) divided by total number of fetuses examined (denominator).  
NA – data not available. Of the 9 B6 dams implanted with D2 embryos, three were treated with maltose, but none had any implants or live pups.

**Fetal transfers across mouse strains which are genetically identical**

**Note that B6 fetuses are very susceptible to alcohol-induced malformations regardless of genotype of mother.**

**D2 fetuses have increased susceptibility when transferred to a B6 mother.**



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# C. Alcohol and Genetics

- So what does this mean?
- The genetics of the fetus and the genetics of the mother determine the impact of alcohol's toxicity during development.
- Some of the genes determining toxicity have been determined but the full determination is not understood.
  - Since we do not understand the genetics fully and we do not do genetic screening of the fetus and mother, we cannot say who is going to be sensitive to alcohol's effects and who is not.

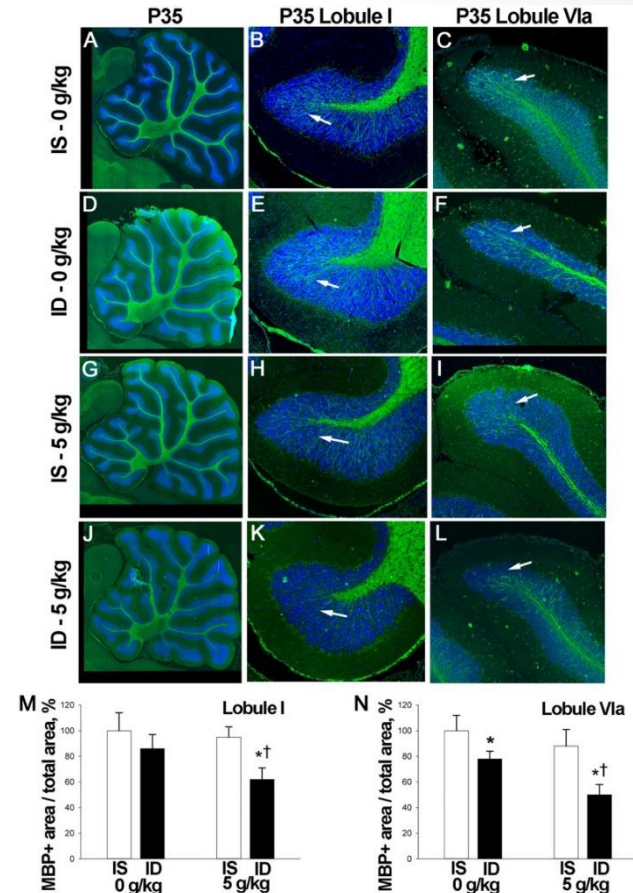


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# D. Alcohol and Other Factors

- Nutrition
  - Inadequate nutrition interacts with alcohol exposure increasing the impact on the fetus.
    - Iron deficiency without anemia (most common nutritional deficiency in pregnancy; 22% of all women of child-bearing age)
    - Choline deficiencies
    - General malnutrition



Rufer et al., 2012: Impact of iron deficiency and fetal alcohol exposure on myelination in the cerebellum in rats

# D. Alcohol and Other Factors

- Prenatal Stress

- Difficult to define but high levels of anxiety during pregnancy are estimated at 8.5%
  - O'Connor et al., 2003 showed that children whose mothers experienced high levels of anxiety in later pregnancy have high rates of persistent behavioral/emotional problems
  - Prenatal stress can also include immune challenge which is increasingly being shown to impact development of the fetus and particularly brain development.
- Interactions with fetal alcohol exposure and prenatal stress remain to be fully understood but are likely.



# D. Alcohol and Other Factors

- Alcohol and other drugs of abuse

- Indications of deleterious interactions of alcohol and
  - Nicotine
  - Stimulants such as cocaine, crack and methamphetamine
  - Caffeine



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# D. Alcohol and Other Factors

- **Postnatal Environment**
  - Development is an on-going process and various perturbations can cause synergistic effects which can be positive or negative on outcome.
  - The postnatal environmental factors are likely to be most important for fetal alcohol effects.
  - There are known positive impacts of environmental enrichment, behavioral interventions, nutritional interventions.
  - There are known negative impacts of impoverished environment, malnutrition, stress, and immune challenges.



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# E. Summary

- Alcohol can cause birth defects ranging from subtle to severe.
- The degree of alcohol-induced damage to the fetus is a function of blood alcohol level which is determined by individual factors and how people drink.
- The degree of alcohol-induced damage to the fetus is also determined by genetics of mother and fetus, nutritional status, level of prenatal stress, use of other drugs, and postnatal environment.



# E. Summary

- Given that a pregnant woman does not know how she metabolizes alcohol, her and her baby's genetic vulnerability, her specific nutritional status, her specific reaction to stressors, her immune challenges, or the potential postnatal environment of her baby, the answer to the question “How much alcohol can a woman drink during pregnancy and be sure to not harm her baby?” is

**None.**

# Useful Links for resources

- TIP Webinar from FASD Center for Excellence
- <http://fasdcenter.samhsa.gov/webinars/TIPWebinar.aspx>
- Free Downloads of TIP 58 (describes best practices in prevention and intervention for FASD) and Literature review
- <http://stores.samhsa.gov>
- CDC FASD Homepage
- <http://www.cdc.gov/ncbddd/fasd/index.html>
- National Organization on Fetal Alcohol Syndrome (NOFAS)
- <http://www.nofas.org>

# Thank you!

# Questions?

# The Arc's FASD Prevention Project

[www.thearc.org/FASD-Prevention-Project](http://www.thearc.org/FASD-Prevention-Project)

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