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Newborn Phosphatidylethanol Screening to Detect Fetal Alcohol Exposure in Uruguay

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Disclosure

- I am not discussing any commercial products or services
- I have no financial interests herein
- I am in compliance with HIPAA in this presentation

Objectives

- Identifying infants or children at risk for developing FASD often relies on confirmation of maternal drinking during pregnancy or detection of prenatal alcohol exposure in the newborn.
- Prenatal records can often lack information on alcohol use.
- In certain situations, maternal self-report can be unreliable due to recall bias or apprehension of stigmatization associated with drinking during pregnancy.
- Biomarkers of alcohol use and/or alcohol exposure can help in identifying at-risk mothers and also newborns who have been exposed to alcohol in utero.
- Phosphatidylethanol is a highly sensitive biomarker of alcohol use but the clinical utility of PEth as a screening test for prenatal alcohol exposure in newborns has not been examined.

Uruguay





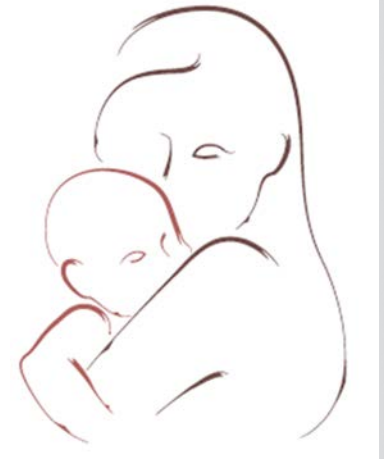
- Cultural patterns of drinking alcohol in Uruguay have changed in the last 30 years, from moderate consumption with meals to more risky patterns of heavy alcohol consumption.
- Drinking during pregnancy is common in Uruguay, in part due to a lack of information given to pregnant women about possible alcohol-related risks from drinking during pregnancy.
- National surveys do not assess alcohol consumption during pregnancy in Uruguay, although recent epidemiological studies have demonstrated that it is a significant problem.



Studies of Alcohol Use during Pregnancy

- In a 2005 study of 900 women surveyed from two public healthcare hospitals in Montevideo following delivery, 36.8% of the mothers reported alcohol consumption at some point during their pregnancy.
- A subsequent study in 2007 found very high rates of reported alcohol consumption (65.6%) in an urban population of young, incompletely educated women from low socioeconomic status delivering in the public healthcare hospitals in Montevideo.
- The incidence of prenatal alcohol exposure, as determined by fatty acid ethyl esters (FAEE) detection in meconium, was found to be 44%.

Study Rationale



- No study to date has examined neurocognitive profiles and facial dysmorphology in a cohort of infants with known alcohol exposure measured in mothers and newborns using a direct alcohol biomarker at birth.

Design

Within 48 Hours
of Birth

- Hospital General de las Fuerzas Armadas in Montevideo, Uruguay
- Maternal Interview 696 mother/newborn pairs
- Mother and baby blood samples for PEth analysis

Six Months

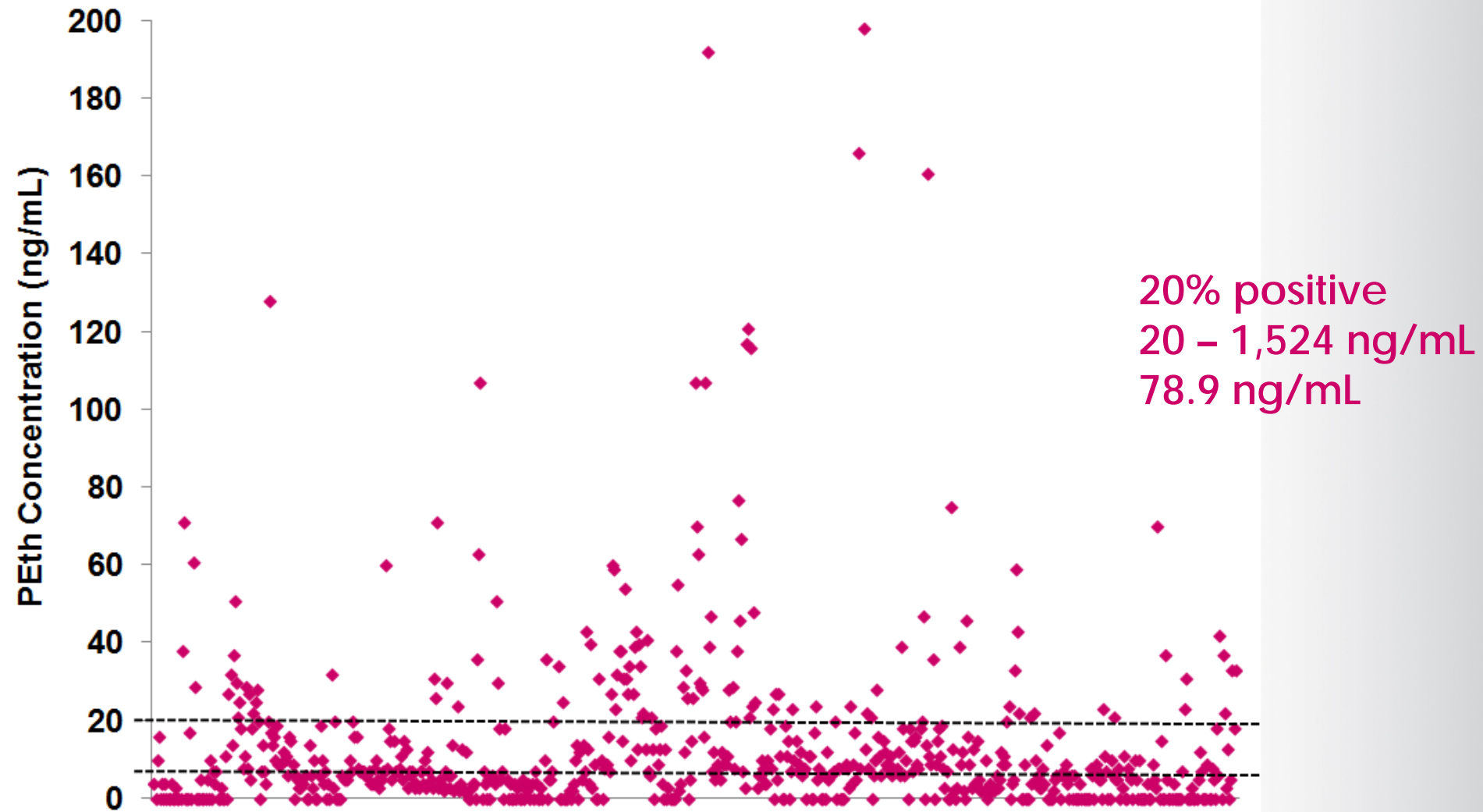
- 41 infants enrolled in follow-up pilot study
- Dysmorphology Checklist
- Bayley Scales of Infant Development
- Vineland Adaptive Behavior

Nine months to
One year

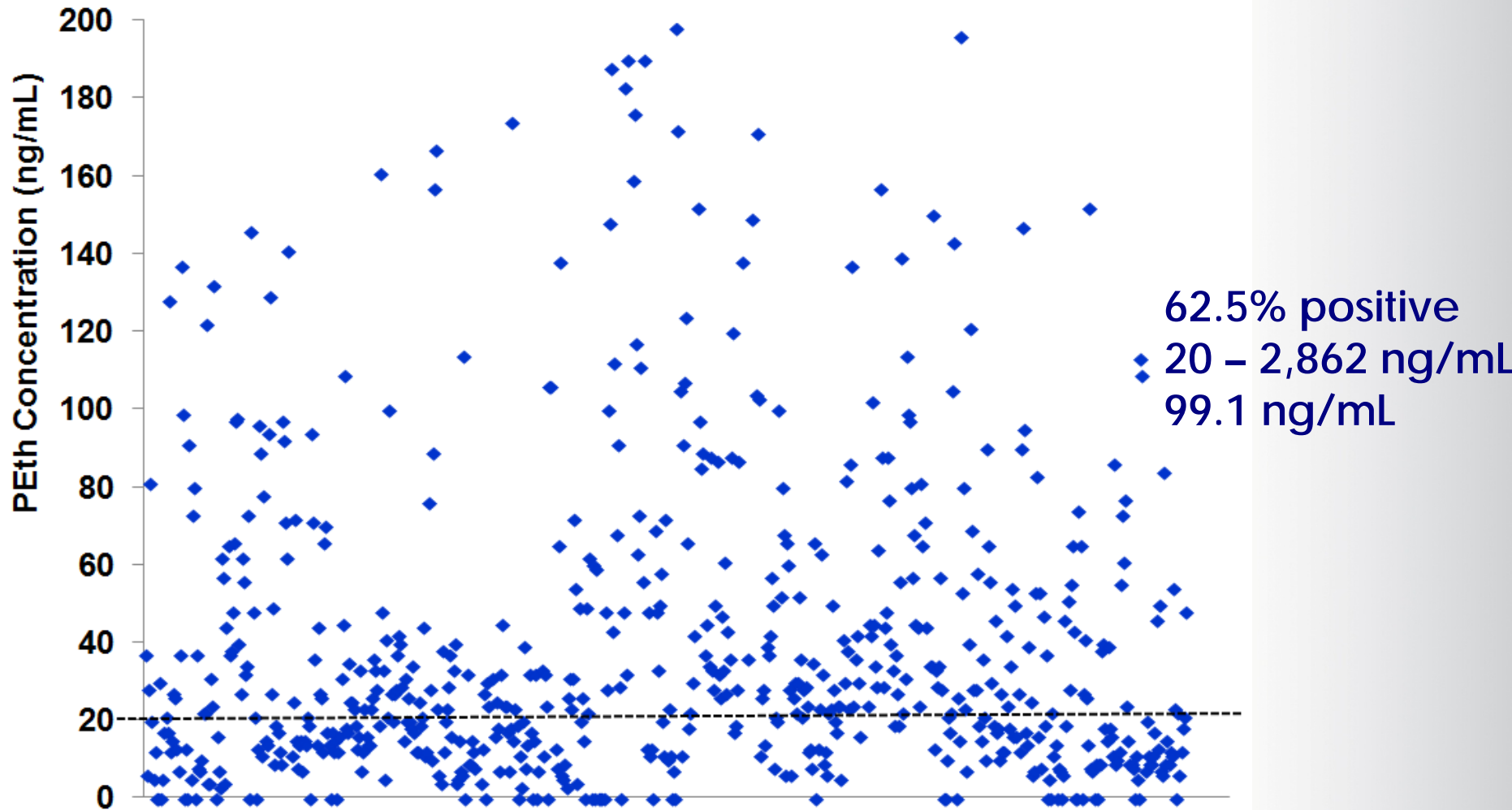
- Dysmorphology Checklist
- Bayley Scales of Infant Development
- Vineland Adaptive Behavior

Biomarker Results

Prevalence of PEth in all enrolled mothers



Prevalence of PEth in all enrolled newborns



Follow Up Study Results

Sample Characteristics in Follow Up Pilot Study (N=41)

Age

Range: 19-40 years

M=27.96 (5.57)



White=46.3%

Black=7.3%

Mixed= 41.5%

Native Uruguayan= 4.9%

Married= 36.6%

Unmarried, partnered= 56.1%

Single =4.9%

Divorced/Separated= 2.4%

Education

M=10.95 (3.34)

Range= 3-21 years



Substance Use During Pregnancy



7.3% at any point in pregnancy
4.9% last 30 days



0% cocaine or marijuana use

Alcohol Use During Pregnancy

Self-Report

First Trimester= 25%

Second Trimester= 4.9%

Last Trimester= 9.8%

Any point in pregnancy = 26.8%



Maternal PEth

Positive =29.3%

Negative= 56.1%

Missing= 14.6%

Average PEth= 34.58ng/mL

Range= 8 -128 ng/mL

Maternal Risk Factors for Alcohol Consuming and Abstaining Women

Difference in Risk Factors by Maternal PEth Result

	Positive Maternal PEth M (SD)	Negative Maternal PEth M (SD)	t	t-test df	p
Age (years)	29.84 (5.20)	27.36 (5.94)	-1.12	33	0.293
Education (years)	11.67 (2.74)	10.95 (3.5)	0.605	30	0.55
Gavidity	3.0 (1.6)	2.09 (1.13)	-1.97	33	0.057
Age at first drink (years)	14.78 (4.46)	16.18 (3.16)	1.07	32	0.292
Heel PEth (ng/mL)	110.0 (92.56)	24.85 (11.62)	-3.16	11.32	0.009
Cord PEth (ng/mL)	79.67 (109.94)	37.93 (23.71)	-1.38	21	0.18

Birth Data

Gestational Age
M = 38.78 weeks

Assigned Sex at Birth
Female = 56.1%
Male = 43.9%

Apgar
1 min: M= 8.82
(0.61)
5 min: M= 9.92
(0.36)



Birth Weight
M= 3295.56g (579.89g)
Range= 1195-4330g

Birth Length
M= 48.84cm (2.18)
Range= 43-54cm

Head
Circumference
M= 34.61cm (1.22)
Range= 32-37

Infant Biomarker Results

Umbilical Cord Blood PEth

Positive= 63.4%
Negative= 9.8%
Missing= 26.8%



Mean Positive PEth= 54.9ng/mL

Range= 13 - 367ng/mL

Heel Stick Blood PEth

Positive= 65.9%
Negative= 14.6%
Missing= 19.5%

Mean Positive PEth= 61.8 ng/mL

Range= 8 - 281ng/mL

Infants Meeting FASD Criteria

Infant	Timepoint		Positive for Alcohol Use				Height ≤ 10%	Weight ≤ 10%	Head Circumference ≤ 10%	Dysmorphology PFL ≤ 10%	Other Significant Dysmorphology	Vermilion Code 4 or 5	Philtrum Code 4 or 5	Bayley ≤ 25%			Vineland ≤ 25%		Diagnosis		
	1	2	Heel PEth	Cord PEth	Maternal PEth	Self-Report								Cognitive	Language	Motor	Communication	Daily Living Skills	Socialization	Motor	ABC
6001	X	X	40	X	X																
6002	X	X	26	X																	
6003	X	X	23																		
6008	X	X	10																		X
6009	X	X	137																		X
6012	X	X	62	X	X	X															X
6014	X	X	14	X	X																
6015	X	X	14	X	X																
6016	X	X	129	X	X																
6018	X	X	15	X																	
6020	X	X	45	X																	
6021	X	X	19		X																
6022	X	X	23	X	X	X															X
6024	X	X	14	X																	
6025	X	X	28	X																	
6027	X	X	42	X		X															X
6033	X	X	167	X	X	X															X
6038	X	X	0																		
6039	X	X	15		X																
6040	X	X	281	X	X																
6041	X	X	207	X	X																
6044	X	X	X																		
6047	X	X	15	X																	
6053	X	X	174	X																	

✓24 infants met the criteria for any FASD diagnosis at either 6 months or 1 year.

✓At the first follow-up 17 children met the diagnostic criteria, with the most common diagnosis being ARND in 16 of the infants.

✓At the second follow-up there were 15 children that met criteria for an diagnosis with ARND again being the most common diagnosis in 12 of the children.

✓No child met the criteria for FAS at either time point.

✓Of the 24 children that met the criteria for an FASD diagnosis at either time point, only 2 children did not have confirmed alcohol exposure during pregnancy based on PEth at birth or maternal self-report.

✓The average PEth concentration at birth in newborns who met the criteria for an FASD diagnosis was 65.2 ng/ml.

Infants Not Meeting FASD Criteria

Infant	Timepoint		Positive for Alcohol Use				Dysmorphology				Bayley ≤ 25%			Vineland ≤ 25%				Diagnosis							
	1	2	Heel PEth	Cord PEth	Maternal PEth	Self-Report	Height ≤ 10%	Weight ≤ 10%	Head Circumference ≤ 10%	PFL ≤ 10%	Other Significant Dysmorphology	Vermilion Code 4 or 5	Philtrum Code 4 or 5	Cognitive	Language	Motor	Communication	Daily Living Skills	Socialization	Motor	ABC	FAS	PFAS	ARND	None
6004	X	X	12											X			X			X					X
6005	X	X	8	X		X								X	X						X				X
6006	X	X	22	X		X	X		X	X				X	X										X
6010	X	X					X							X	X	X									X
6013	X	X	27				X																		X
6017	X	X	21	X	X	X			X						X										X
6023	X	X	7	X			X																		X
6028	X	X	37						X																X
6031	X	X	25	X					X																X
6032	X	X					X		X	X				X	X	X		X		X					X
6034	X	X	157	X	X				X	X															X
6035	X	X	157	X	X		X			X															X
6036	X	X	29	X		X			X																X
6037	X	X	6											X											X
6048	X	X	24	X					X	X															X
6049	X	X	24	X			X	X	X	X															X
6050	X	X	7							X															X

- ✓ 17 children did not meet the criteria for an FASD diagnosis at 6 months or 1 year time points.
- ✓ Only 3 of the mothers had a positive PEth at the time of birth, compared to 11 of the mothers who had a child that did meet the criteria for an FASD.
- ✓ The average PEth concentration at birth in newborns who did not meet the criteria for an FASD diagnosis was 37.5 ng/ml.

Discussion and Conclusions

- These findings suggest that the prevalence of alcohol consumption during pregnancy continues to be a serious public health problem in Uruguay.
- These findings also suggest that biomarker screening can assist in early infancy developmental and dysmorphology testing to screen for FASD.
- Early identification is key for early intervention, and newborn PEth screening could assist in identify prenatal alcohol exposure.

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