

## Fetal Alcohol Spectrum Disorders

### From Discovery to Prevention

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## Fetal Alcohol Syndrome

What is FAS?

- Growth deficiency** (ht or wt below the 10<sup>th</sup> percentile)
- CNS damage** (evidence of structural, neurological or functional impairment)
- Unique cluster of minor facial anomalies** (small eyes, smooth philtrum, thin upper lip)
- Prenatal alcohol exposure**

Prevalence: 1 to 3 per 1,000 live births (equivalent to down syndrome).  
Leading known cause of mental retardation / developmental disabilities.  
Entirely preventable.

### What is Fetal Alcohol Spectrum Disorders (FASD)?

- **FASD** is an umbrella term that refers to the full spectrum of outcomes observed among individuals with prenatal alcohol exposure.
- FASD is **NOT** a diagnostic term. An individual would **NOT** receive a diagnosis labeled FASD. The term is too broad to serve as a meaningful diagnostic category.
- Diagnoses that fall under the umbrella of FASD include **FAS, partial FAS, and Alcohol Related Neurodevelopmental Disorders (ARND)**.
- Generally speaking: Partial FAS is "FAS without the growth deficiency". ARND is "FAS without the FAS facial features".
- The prevalence of ARND is far greater than FAS. The magnitude of CNS damage is comparable.

### Discovery of FASD

- 1968:** Discovered by Christy Ulleland, M.D., Chief Resident, Harborview Medical Center, Seattle WA.
- 1968:** Independently discovered in France by Lamoine.
- 1973:** The term FAS is coined by David Smith, M.D., Professor of Pediatrics, University of Washington.
- 2004:** The umbrella term FASD is coined.

### FASD 4-Digit Diagnostic Guide, Software, and Training

Training  
4-Digit Online Course  
Diagnostic Team Training

All Diagnostic Tools and Courses available at cost or free on the web.  
[www.fasdpn.org](http://www.fasdpn.org)

### The FASD 4-Digit Diagnostic Code

		<b>3</b>	<b>4</b>	<b>3</b>	<b>4</b>	
R a n k	4	≤ 2 %	All 3 features	Structural / Neurological Abnormalities	Confirmed High	4
	3	3 - 5 %	2 features	Severe Dysfunction	Confirmed Moderate	3
	2	6 - 10 %	1 feature	Moderate Dysfunction	Unknown	2
	1	> 10 %	No features	No Dysfunction	Confirmed Absent	1
		Growth	Face	CNS	Alcohol	

### The FASD 4-Digit Diagnostic Code

				<b>3</b>	<b>4</b>	<b>4</b>	<b>4</b>		
significant	severe	definite	4		X	X	X	4	high risk
moderate	moderate	probable	3	X				3	some risk
mild	mild	possible	2					2	unknown
none	none	unlikely	1					1	no risk
				Growth	Face	CNS	Alcohol		
Growth Deficiency	FAS Facial Features	CNS Damage							Prenatal Alcohol

### Example of 4-Digit Codes for FAS and Partial FAS

**A Fetal alcohol syndrome (alcohol exposed)**

2433	3433	4433
2434	3434	4434
2443	3443	4443
2444	3444	4444

**B Fetal alcohol syndrome (alcohol exposure unknown)**

2432	3432	4432
2442	3442	4442

**C Partial fetal alcohol syndrome (alcohol exposed)**


1333	1433	2333	3333	4333
1334	1434	2334	3334	4334
1343	1443	2343	3343	4343
1344	1444	2344	3344	4344


### The FAS Face Across Race and Age

Photos removed

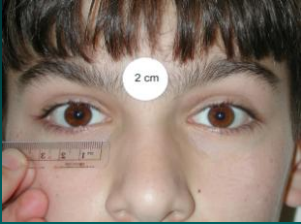

### Three FAS Facial Features

- 1) PFL  $\leq -2$  SD
- 2) Lip Rank 4 or 5
- 3) Philtrum Rank 4 or 5







### Two methods to measure Palpebral Fissure Length

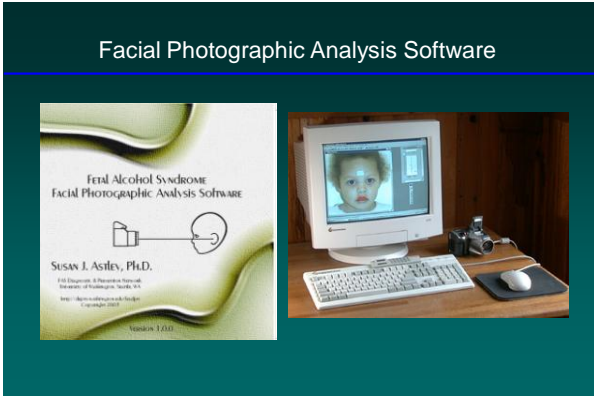
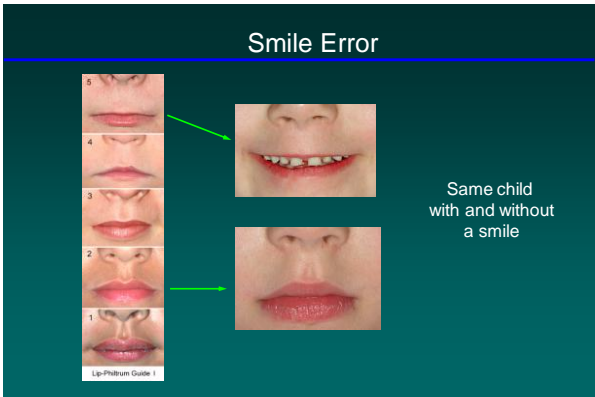
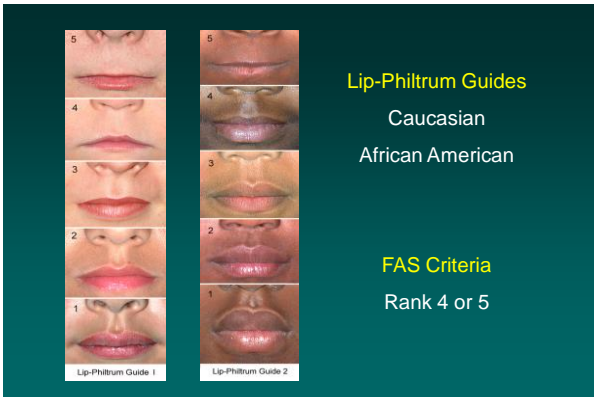



1. Measure eye directly using ruler. Confirm accuracy of physician's measurement technique by practicing on an eye measured with calipers.
2. Measure eye in digital photo using FAS Facial Analysis Software.

### Two Methods to Measure Lip Thinness

1. Measure directly with Lip-Philtrum Guide. Physician should be aligned in patient's frankfort horizontal plane.
2. Measure lip circularity (perimeter<sup>2</sup>/area) from digital photograph using FAS Facial Analysis Software.



**FAS Screening, Diagnosis, Prevention and Surveillance**

To implement and assess prevention efforts, one must be able to accurately and efficiently screen, diagnose and intervene with high-risk populations.

In Washington State this has been accomplished through the establishment of:

- PRAMS data collection (1993)
- WA State FAS Diagnostic & Prevention Network of Clinics (1993)
- FASD Facial Photographic software (1995)
- FASD 4-Digit Diagnostic Code (1997)
- Foster Care FAS Screening Program (1999)

**FAS Screening in Foster Care using Facial Photographs**

Results

FAS Prevalence	1 per 100
Participation Rate	98 %

Screening Tool Performance

Sensitivity	100 %
Specificity	99.8 %
Predictive Value Positive	86 %
Predictive Value Negative	100 %

**Evidence of FAS Prevention in Washington State**

PRAMS Data (1993-98)

Maternal report of drinking during pregnancy

Significant decline in maternal drinking during pregnancy from 1993 to 1998.

Exceeded Health People 2010 goal of 6% in 1997.

Prevalence of FAS in Foster Care

Among children born in 1993 – 1998.

Significant reduction in prevalence of FAS in each successive birth cohort from 1993 to 1998.

## MRI, MRS, and fMRI in Children with FAS/D

### Preliminary Findings

Washington State  
 FAS Diagnostic & Prevention Network  
 FAS DPN  
 University of Washington

Susan J. Astley Ph.D.  
 Professor and Director

### FASD MRI, MRS, fMRI Study: Preliminary Findings

Primary Hypotheses

The following will differ between children with FAS/D and typically developing children:

- neuro-structure (size of specific brain structures)
- neuro-function (as measured by psychological, psychiatric, and fMRI assessment)
- neuro-chemistry (neurometabolites: choline and n-acetyl-aspartate)

Are the neuro-structural, neuro-functional and neuro-chemical impairments inter-correlated?

Long-range Clinical Question

Can MRI, MRS, and/or fMRI improve the accuracy of a FASD diagnostic evaluation?

### FASD MRI, MRS, fMRI Study

STUDY POPULATION

Four groups (8-15 years old)

1. FAS / Partial FAS (n = 20)
2. Static Encephalopathy / Alcohol Exposed (SE/AE) (n = 24)  
(no FAS facial features) Brain Rank 3 or 4 (equivalent to Severe "ARND")
3. Neurobehavioral Disorder / Alcohol Exposed (ND/AE) (n = 21)  
(no FAS facial features) Brain Rank 2 (equivalent to Mild "ARND")
4. Controls (n = 16)  
(typical development, No alcohol exposure)

### FASD MRI, MRS, fMRI Study: Methods


MRI: Structure

Volumes

- caudate
- putamen
- hippocampus
- frontal lobe
- frontal gray matter
- frontal white matter
- total brain

Midsagittal Area

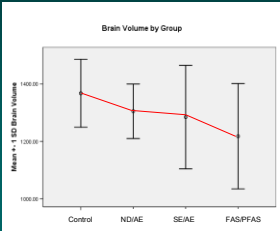
- corpus callosum
- cerebellar vermis
- total brain



### FASD MRI, MRS, fMRI Study: Results

Key Structural Findings

All brain regions become progressively smaller (absolute size) as you advance across the 4 Diagnostic Groups from Group 4 (Controls) to Group 1 (FAS / PFAS).

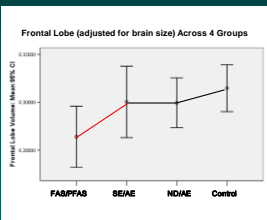


Group	Mean Brain Volume (approx.)
Control	1400
ND/AE	1350
SE/AE	1320
FAS/PFAS	1250

### FASD MRI, MRS, fMRI Study: Results

Key Structural Findings

The frontal lobe is significantly smaller in FAS/PFAS relative to Severe ARND, Mild ARND, and Controls, even after adjustment for overall brain size.



Group	Frontal Lobe Volume (Mean +/- 1 SD) (approx.)
FAS/PFAS	0.0025
SE/AE	0.0035
ND/AE	0.0035
Control	0.0040

### FASD MRI, MRS, fMRI Study: Results

**Key Structural Findings**

The caudate is significantly smaller in both FAS/PFAS and Severe ARND, relative to Mild ARND and Controls, even after adjustment for overall brain size.

Group	Caudate Volume (Mean and 95% CI)
FAS/PFAS	~0.00025
SE/AE	~0.00020
ND/AE	~0.00055
Control	~0.00065

### FASD MRI, MRS, fMRI Study: Results

**Key Structural Findings**

Brain function decreases with decreasing size of brain regions.

One global measure of brain function is the 4-Digit Brain Rank:

- Rank 1 (normal function)
- Rank 2 (mild impairment)
- Rank 3 (severe impairment)

4-Digit Brain Functional Rank	Mean +/- 1 SD Caudate Volume
1 (Normal)	~9.5
2 (Mild Impairment)	~8.5
3 (Severe Impairment)	~7.5

### FASD MRI, MRS, fMRI Study: Results

**Key Structural Findings**

Some functional impairments appear correlated with reduction in specific brain regions.

ADHD	Frontal Lobe Volume (Mean and 95% CI)
No	~425.00
Yes	~375.00

ADHD	Putamen Volume (Mean and 95% CI)
No	~1.50
Yes	~1.40

### FASD MRI, MRS, fMRI Study: Results

**Key Structural Findings**

Percent of subjects with one or more brain regions significantly smaller than Control group.

FAS/PFAS (CNS Rank 3 with FAS facial features)	70%
SE/AE (CNS Rank 3, No FAS facial features)	58%
ND/AE (CNS Rank 2, No FAS facial features)	43%
Controls (CNS Rank 1, No FAS facial features)	0%

Thus, as level of dysfunction increases from Rank 1: none, to Rank 2: mild, to Rank 3: severe, the risk of underlying structural abnormality increases significantly.

Even subjects with neurobehavioral disorder have underlying structural abnormality.

### FASD MRI, MRS, fMRI Study: Results

**Key Facial Findings**

The frontal lobe decreases in size as the 4-Digit FAS face becomes more severe.

Frontal lobe and the FAS face both share the same embryologic origin (frontonasal prominence).

4-Digit Face Rank	Frontal Lobe Volume (CC mean, 95% CI)
1. None	~425
2. Mild	~390
4. Severe	~355

### FASD MRI, MRS, fMRI Study: Results

**Key Facial Findings**

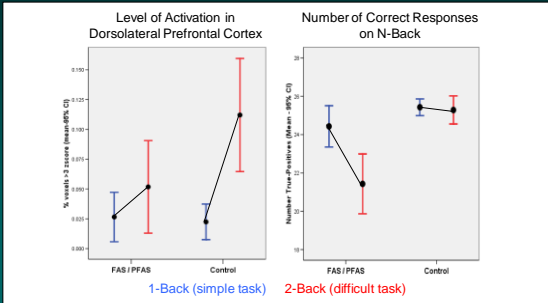
The more severe the FAS facial features, the more severe the impairment in brain function.

4-Digit Face Rank	Mean +/- 1 SD WISC FSIQ
1 (None)	~105
2 (Mild)	~95
3 (Severe)	~85

4-Digit Face Rank	Mean +/- 1 SD Rey Delayed Recall (Total)
1 (None)	~45
2 (Mild)	~40
3 (Severe)	~35

FASD MRI, MRS, fMRI Study: Results

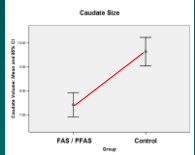
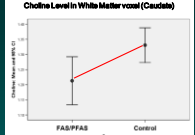
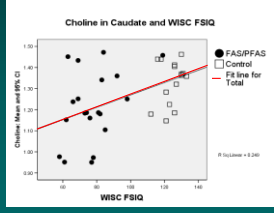
One of Several fMRI Findings: Activation and Working Memory



FASD MRI, MRS, fMRI Study: Results

One of Several Spectroscopy Findings

- Choline is significantly lower among FAS / PFAS.
- Caudate is significantly smaller in FAS / PFAS.
- Low choline is significantly associated with low IQ.



FAS DPN Website

All Publications, Diagnostic Tools, Guides and Training Programs  
Can be found on our website

[www.fasdpn.org](http://www.fasdpn.org)