# Neurobiology of Risk and Resilience of Children with Suspected Fetal Alcohol Spectrum Disorders (FASD)

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## Objectives

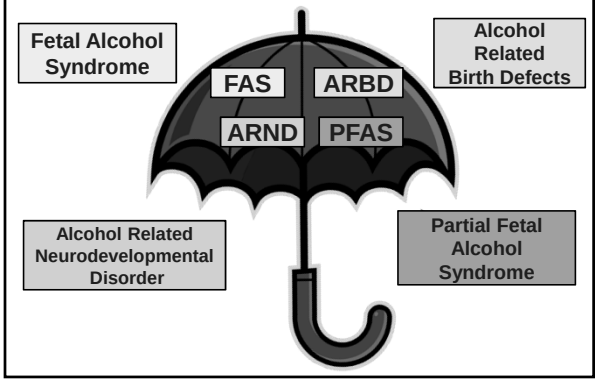
1. To review the diagnostic classification of Fetal Alcohol Spectrum Disorders (FASD)
2. To review the diagnostic criteria of FAS
3. To highlight the effects of intrauterine alcohol exposure on the developing brain (structural and functional changes in the brain)
4. To discuss opportunities to promote resilience in children with FASD.

## 1. Classification of FASD's

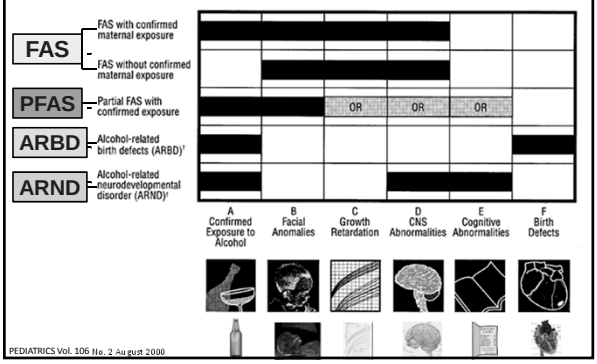

## What is Fetal Alcohol Syndrome?

- Preventable birth defect caused by maternal alcohol consumption during pregnancy
- Characterized by physical, cognitive and behavioral abnormalities
  - Many abnormalities are a reflection of damage that was done to the brain of the developing fetus
- Results in lifelong impairments

## The Umbrella of FASD




## Spectrum of FASD



## Fetal Alcohol Syndrome (FAS)
### Diagnostic Criteria

- Confirmed Maternal Alcohol Exposure
- Abnormal Facial Features
  - Short palpebral fissures
  - Smooth philtrum
  - Thin vermillion border
- Growth deficiencies
  - Height or weight <10%
- CNS Dysfunction
  - Structural
  - Neurological
  - Microcephaly

*American Family Physician*

*July 15, 2005 Volume 72, Number 2*

PEDIATRICS Vol. 115 No. 1 January 2005

## Partial Fetal Alcohol Syndrome (PFAS)

- Confirmed Maternal Alcohol Exposure
- Abnormal Facial Features (≥2)
  - Short palpebral fissures
  - Smooth philtrum
  - Thin vermillion border

**AND** ONE OR MORE OF THE FOLLOWING:

- Growth deficiencies
  - Height or weight <10%
- CNS Dysfunction
  - Structural
  - Neurological
  - Microcephaly
- Complex Pattern of Behavior or Cognitive Abnormalities

PEDIATRICS Vol. 115 No. 1 January 2005

## Alcohol Related Birth Defects (ARBD)

- Confirmed Maternal Alcohol Exposure
- Abnormal Facial Features (≥2)
  - Short palpebral fissures
  - Smooth philtrum
  - Thin vermillion border

**AND**

- One or more congenital defects:
  - Malformations or Dysplasias
    - Heart
    - Lungs
    - Bone
    - Kidneys
    - Vision
    - Hearing System

**OR**

- Two or more minor anomalies



Alcohol Research & Health Vol. 25, No. 3, 2001

PEDIATRICS Vol. 106 No. 2 August 2000

PEDIATRICS Vol. 115 No. 1 January 2005

## Alcohol Related Neurodevelopmental Disorder (ARND)

- Confirmed Maternal Alcohol Exposure

AND 1 of the following:

- CNS Neurodevelopmental Abnormalities
  - Microcephaly at birth
  - Structural brain abnormalities
  - Neurological hard signs

OR

- Complex pattern of behavioral or cognitive deficits

*(*inconsistent with developmental level, and unexplained by genetic background or environmental conditions*)*

**TERATOLOGY 56:317–326 (1997)**

Alcohol Research & Health Vol. 25, No. 3, 2001

PEDIATRICS Vol. 115 No. 1 January 2005

## Cognitive and Behavioral Abnormalities in FASD

- Complex pattern of behavioral or cognitive deficits

*(*inconsistent with developmental level, and unexplained by genetic background or environmental conditions*)*

  - Learning disabilities
  - Deficits in school performance
  - Poor impulse control
  - Problems in social perception
  - Language deficits
  - Poor capacity for abstraction
  - Specific deficits in mathematical skills
  - Problems in memory, attention or judgment

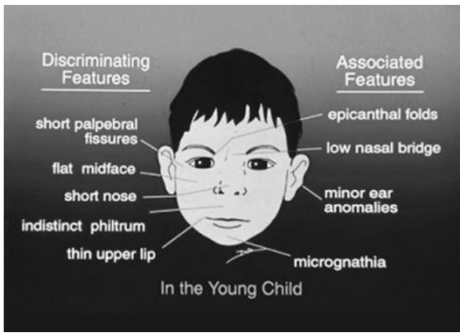
Alcohol Research & Health Vol. 25, No. 3, 2001

**TERATOLOGY 56:317–326 (1997)**

## Diagnosing FASD…..

Edvard Munch : *The Scream, 1893*

## 2. Diagnostic Criteria of FAS

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  - Neurological
  - Functional

Institute of Medicine report on FAS (IOM, '96)
*American Family Physician*
*July 15, 2005 Volume 72, Number 2*
PEDIATRICS Vol. 115 No. 1 January 2005

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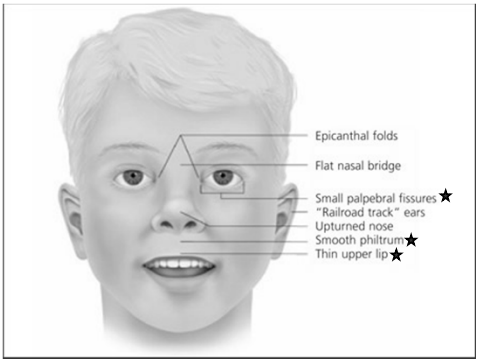
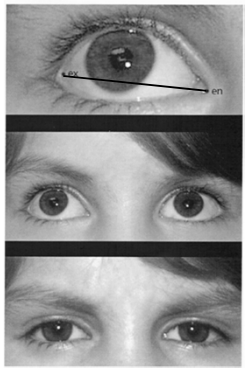
## Dysmorphology in FAS




Am Fam Physician2005;72:279-82, 285

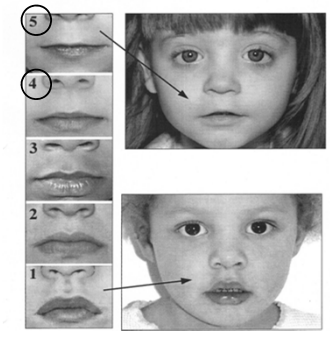
Palpebral Fissure Length




FAS Facial Characteristics

Palpebral Fissure Length (PFL) < 10%

Lip - Philtrum Guide

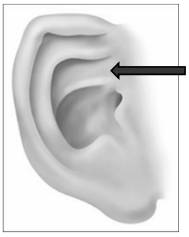



FAS Facial Characteristics

University of Washington Lip-Philtrum Guide Rank 4 or 5 for race)

## Minor Anomalies

- Railroad Track Ears

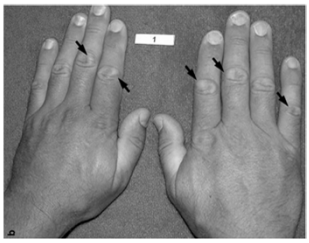



## Minor Anomalies

- Clinodactyly

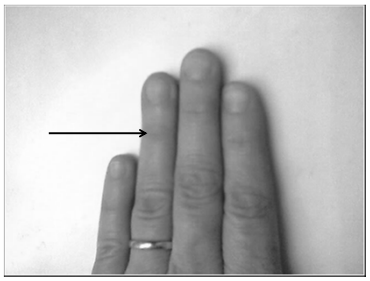

## Minor Anomalies

- Camptodactyly

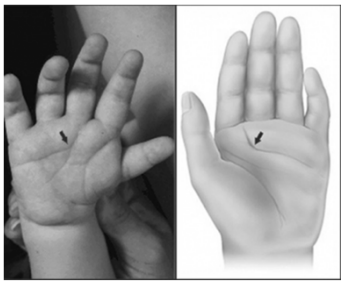
## Minor Anomalies

- Shortened 5th Finger



## Minor Anomalies

- Hockey Stick Palmar Crease



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*July 15, 2005 Volume 72, Number 2*

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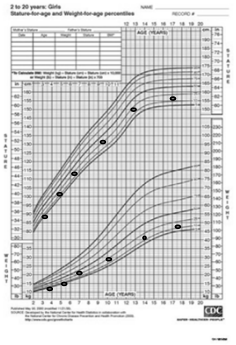
## Growth in FAS

- Prenatal or postnatal height, weight or both <10%
- Documented at any one point in time
- Adjusted for age, sex, gestational age, and race or ethnicity
- Growth deficit is not due to FTT/ endocrine disorder, or environmental factors




CDC, 2005

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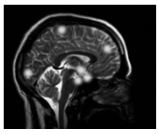
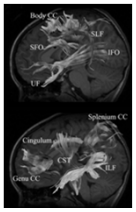
*July 15, 2005* ▯ *Volume 72, Number 2*

PEDIATRICS Vol. 115 No. 1 January 2005

## CNS Abnormalities in FAS

- Structural
  - FOC <10%, adjusted for gender and age
  - Clinically significant brain abnormalities observable through thorough brain imaging (MRI/DTI/PET)
    - Corpus callosum
    - Basal ganglia
    - Cerebellar vermis

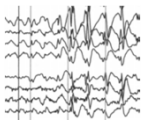


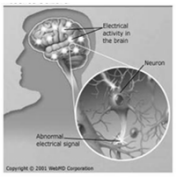



CDC, 2005

## CNS Abnormalities in FAS

- Neurological
  1) Seizures not due to a postnatal insult or fever
  2) Soft neurologic signs
     - Coordination difficulties
     - Visual Motor Problems
     - Nystagmus
     - Difficulty with motor control
  3) Cannot be due to environmental or organic causes

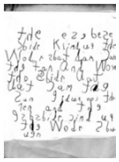





CDC, 2005

## CNS Abnormalities in FAS

- Functional
  a. Global cognitive deficit or significant developmental delay
     - > 2 SD below the mean
     - IQ < 70 (Mental Retardation)

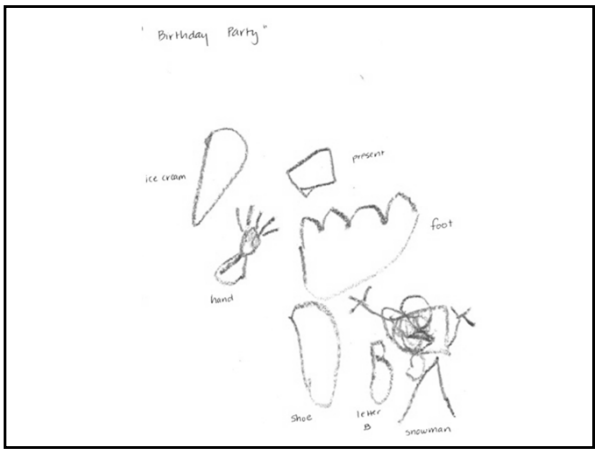


CDC, 2005

## CNS Abnormalities in FAS

- Functional
  b. Deficits in > 3 functional domains
     1. Specific learning disabilities : math/ visuospatial skills
        - Uneven profile of cognitive skills
        - Poor academic achievement
        - Discrepancy between verbal and nonverbal skills
     2. Motor function delays or deficits
        - Visual-motor/ visuo-spatial coordination
        - Delayed motor milestones
        - Difficulty with writing or drawing
        - Clumsiness
        - Balance problems
        - Poor dexterity

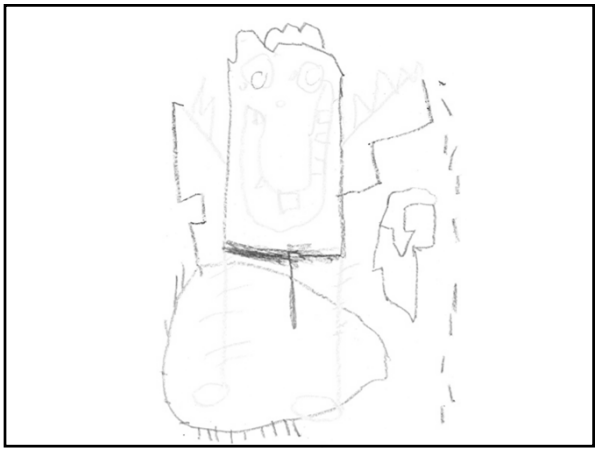
CDC, 2005




## CNS Abnormalities in FAS

- Functional
  - b) Deficits in > 3 functional domains
    3. Executive function deficits:
       - Poor organization and poor planning
       - Limited concrete thinking
       - Lack of inhibition
       - Difficulty grasping cause and effect
       - Inability to delay gratification
       - Difficulty with multistep directions
       - Poor judgement
       - Inability to apply knowledge to new situations

CDC, 2005



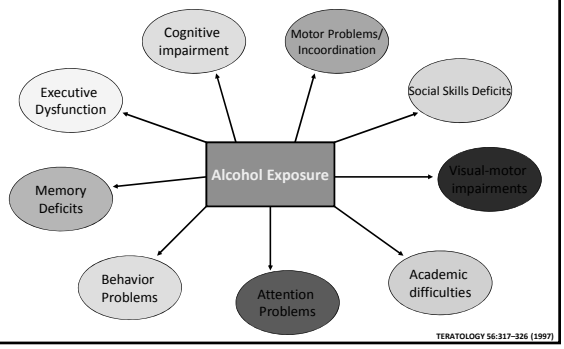
## CNS Abnormalities in FAS

- Functional
  - b. Deficits in > 3 functional domains
    4. Attention and hyperactivity problems
    5. Social skills problems
    6. Sensory sensitivities
    7. Pragmatic language problems
    8. Memory Deficits
       - Forgetting well learned/previously learned material
       - Difficulty responding to common parenting practices

*Deficits in 3 Functional deficits > 1 SD below the mean*

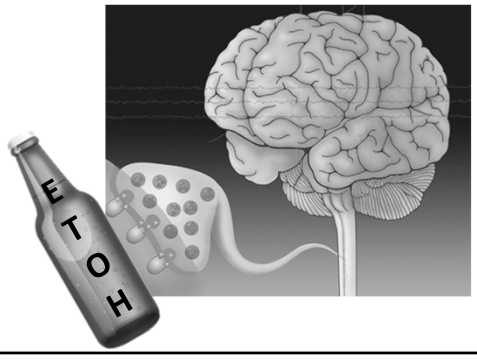
CDC, 2005

## Neurodevelopmental Consequences of Intrauterine Alcohol Exposure

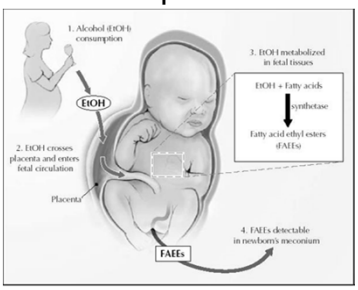



TERATOLOGY 56:317–326 (1997)

## 3. Effects of Alcohol on Brain Development



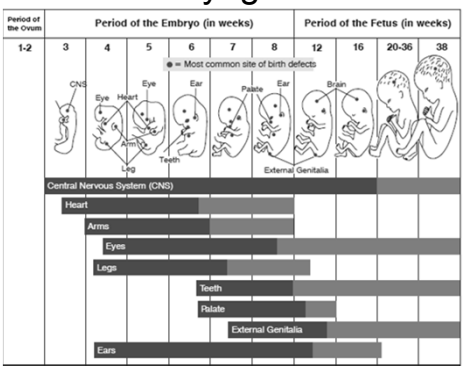
## Intrauterine Effects of Alcohol Exposure




*Effects on the developing fetus are determined by DOSE, DURATION and TIMING*

JAMC, 25 NOV 2003, 169 (11), 1184.

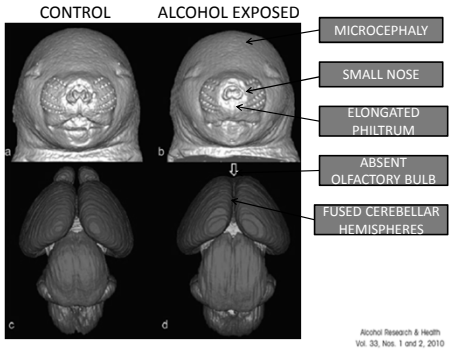
## Embryogenesis




Source: National Organization on Fetal Alcohol Syndrome (NOFAS), 2004; Adapted from Moore, 1993.

## There is no safe time to drink while pregnant

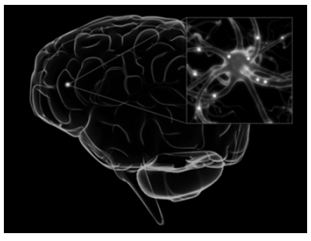

## Facial Dysmorphology : DOL = 17(mouse)




Alcohol Research & Health Vol. 33, Nos. 1 and 2, 2010

## Neurotoxic Effects of Alcohol on the Developing Brain

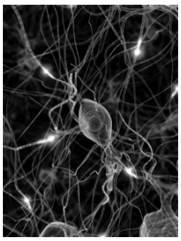
- Neurogenesis
- Cell Growth and Differentiation
- Neuronal Migration
- Synaptogenesis
- Apoptosis
- Plasticity



*Alcohol & Alcoholism*, pp. 1–7, 2009
*FASD Competency-Based Curriculum Development Guide*
CDC, 2005

## Timeline for Neurogenesis

- Neuronal Proliferation:
  - Peak = 2-4 months of gestation
- Migration:
  - Peak = 3-5 months of gestation
- Organization:
  - Peak = 6 months of gestation to several years postnatal
- Myelination:
  - Birth to many years postnatal



*There is no safe time to drink while pregnant*

## Brain Regions Affected by Prenatal Alcohol

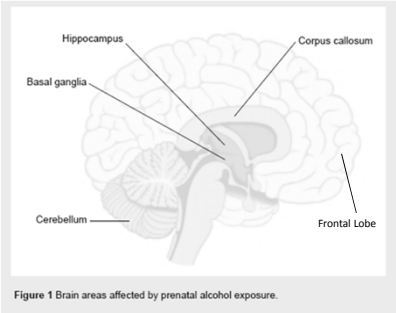
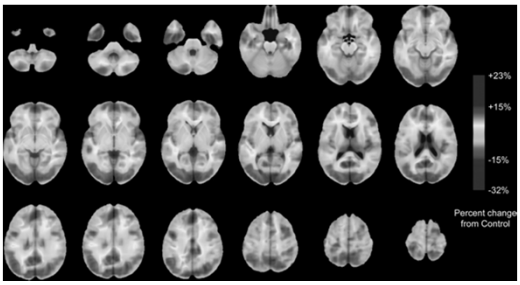



**Figure 1** Brain areas affected by prenatal alcohol exposure.

Alcohol Research & Health Vol. 25, No. 3, 2001

## Brain Regions Affected by Prenatal Alcohol

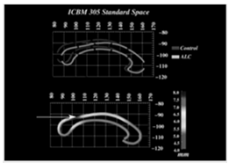
**Alcohol Exposed : Percentage Difference from Average Controls**

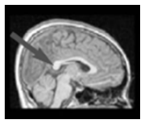



**Sowell, E. R. et al. J. Neurosci. 2010;30:3876-3885**

## Effects of Alcohol on the Corpus Callosum

- Function of C.Callosum: connect right and left hemispheres of the brain
- Effects of Alcohol on Corpus Callosum
  - Partial or complete agenesis of the corpus callosum
  - Hypoplasia or displacement of CC
  - Decreased white matter integrity of the corpus callosum
- *Associated with neuropsychological deficits*
  - *Decreased bimanual coordination*
  - *Impaired verbal learning ability*
  - *Impaired executive and psychosocial function*



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*Alcohol & Alcoholism*, pp. 1–7, 2009

Alcohol Research & Health Vol. 25, No. 3, 2001

## Effects of Alcohol on the Cerebellum

- Function of Cerebellum: Important for motor functions such as posture, balance, and coordination, and attention
- Effects of Alcohol on Cerebellum:
  - Reduced surface area
  - Decreased volume of the cerebellum and anterior cerebellar vermis
  - Displacement of superior and anterior edges of the anterior vermis
- *Associated with certain functional deficits in*
  - *Balance,*
  - *Bimanual coordination*
  - *Attention*
  - *Verbal learning and memory*

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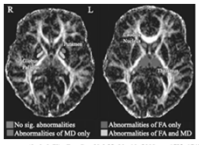
## Effects of Alcohol on the Basal Ganglia

- Function of Basal Ganglia: Includes the caudate nucleus, putamen, and globus pallidus. They are involved in motor abilities and cognitive functions, including executive function
- Effects of Alcohol on Basal Ganglia: Decreased volume of the caudate
- *Associated with certain functional deficits in*
  - *Executive function*
  - *Attention*
  - *Response inhibition -*
    *(i.e. shifting from one task to another)*
  - *Inhibition of inappropriate behavior*
  - *Spatial memory*
  - *Higher cognitive function*




*Alcohol Clin Exp Res*, Vol 32, No 10, 2008: pp 1732-1740

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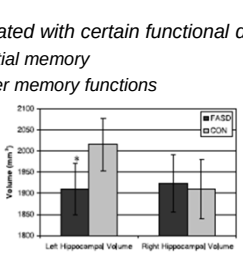
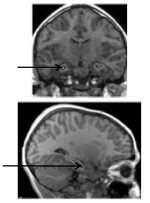
## Effects of Alcohol on the Hippocampus

- Function of Hippocampus: Consolidation of new memory
- Effects of Alcohol on Hippocampus: Decreased volume of the hippocampus ( Greater volume loss on L > R)
- *Associated with certain functional deficits in*
  - *Spatial memory*
  - *Other memory functions*



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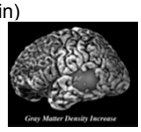
*Journal of the International Neuropsychological Society* (2008), 14, 1022-1033.

## Effects of Alcohol on Cortical Development

- Function of Cortex: Cortex is comprised of gray matter (cell bodies and dendrites) and white matter (axons surrounded by sheaths of myelin) White matter contains the necessary connections for proper cognitive function.
- Effects of Alcohol on Cortex:
  - Decreased white matter volume
  - Abnormalities in white matter tracts
- *Associated with certain functional deficits in*
  - *Cognition*
  - *Motor function*
  - *Attention*
  - *Executive function*





*Alcohol & Alcoholism*, pp. 1–7, 2009
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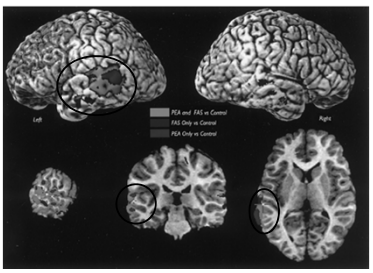
## Effect of Alcohol on Cortical Development

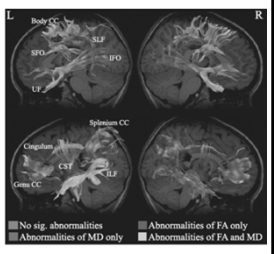
White matter deficits localized to left temporal and parietal lobes




COGNITIVE NEUROSCIENCE AND NEUROPSYCHOLOGY
Vol 12 No 3 5 March 2001

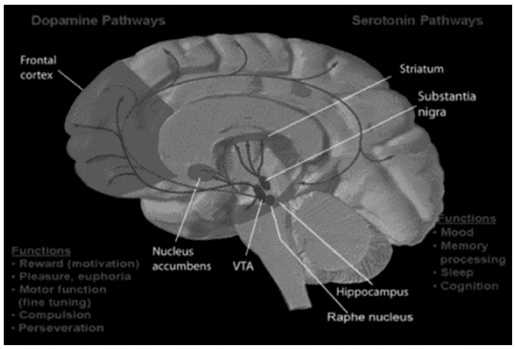
## White Matter Tract Differences : FASD

- Widespread involvement of white matter tracts in children with FAS
- Abnormalities noted in neural pathways involving:
  - Corpus callosum *(bilateral coordination)*
  - Corticospinal tracts *(motor function)*
  - Occipto-temporal tract *(visual processing)*
  - Right cingulum *(connection between temporal and frontal lobes)*

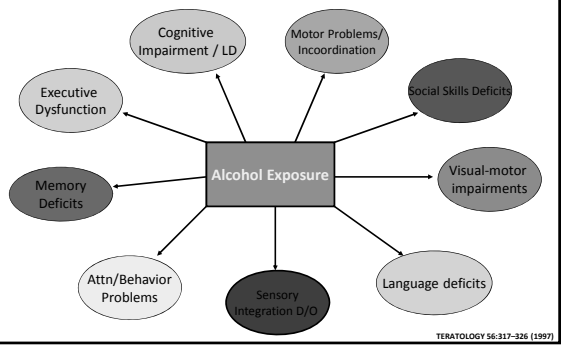



*Alcohol Clin Exp Res*, Vol 32, No 10, 2008: pp 1732–1740

## Neural Pathways Affected in FASD



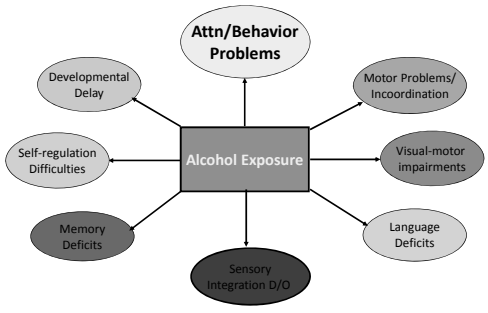

## Neurodevelopmental Consequences of Intrauterine Alcohol Exposure




TERATOLOGY 56:317–326 (1997)

## Neurodevelopmental Consequences of Intrauterine Alcohol Exposure

*Infant –Toddler Symptoms*




TERATOLOGY 56:317–326 (1997)

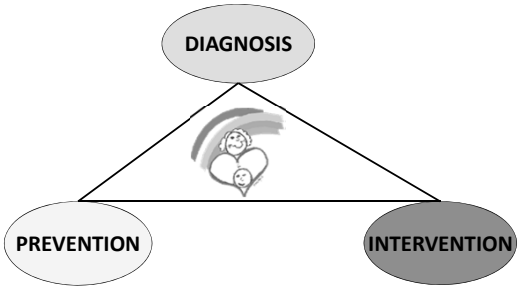
## 4. Case-Based Learning

Could it be...

An F.A.S.D.????

## 5. Optimizing Outcomes in FASD: Promoting Resilience


## Optimizing Outcomes in FASD: Promoting Resilience




## Optimizing Outcomes in FASD

- Promoting Early Diagnosis
  - *"The FAS diagnosis and the diagnostic process…are part of a continuum of care that identifies and facilitates appropriate health care, education, and community services."*
- *Diagnosis is recommended **prior to age 6** to help a child with FAS reach his developmental potential*

*Fetal Alcohol Syndrome: guidelines for referral and diagnosis. (2005). Department of Health and Human Services, p. 22-23*

## Optimizing Outcomes in FASD

- Promoting Early Diagnosis
  - Targeting high risk populations:
  - The CHILD as the point of entry
    - Children of substance abusing mothers
    - Children in foster care
    - Children who are internationally adopted

*The incidence of FAS is 10X higher for children in the foster care system*

## Optimizing Outcomes in FASD

- Promoting Prevention
  - The mother has information to prevent FAS in future births
  - The MOTHER as a point of entry: GOAL: Identify woman who are drinking during pregnancy, and provide them with intervention services
  - *Children who are born to women who STOP drinking in their pregnancy have better outcomes than those who CONTINUE to drink in pregnancy*

CDC, 2005

## Optimizing Outcomes in FASD

- Promoting Intervention : Protective factors
  - Stable and nurturing caregiving environment during the school years
  - Absence of exposure to violence
  - Minimal number of placement / caregiver changes
  - Eligibility for social and educational services


CDC, 2005

## Optimizing Outcomes for Children with FASD

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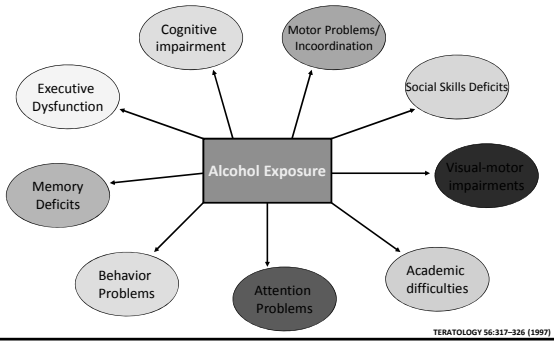
CDC, 2005

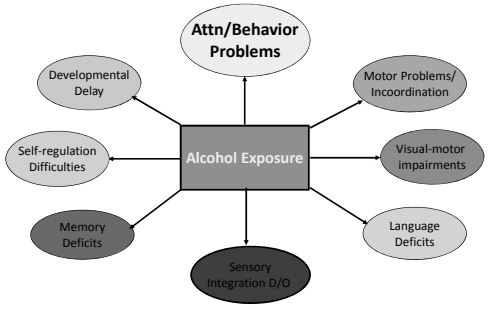
## Indications for Social and Educational Services




TERATOLOGY 56:317–326 (1997)

## Indications for Social and Educational Services

*Infant –Toddler Symptoms*

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CDC, 2005

## Optimizing Caregiver Stability


CDC, 2005

## Optimizing Caregiving Stability



## How do caregiving relationships influence social-emotional development?

⇒ Lessons from attachment theory

## What is Attachment?

- Described by John Bowlby in 1969
- A bond, tie or enduring relationship between a young child and his caregiver
- Occurs by 12 months of age to primary caregiver, regardless of quality of care
- Quality of the attachment relationship varies with the history of the infant's caregiving experiences, and reflects the history of caregiving sensitivity (Sroufe, 1985)
  - Secure vs. Insecure Attachment

## Evolution of Attachment

- Infancy in mammals is characterized as a period of helplessness and vulnerability
- Infant is completely dependent on his caregiver for care and protection
- The attachment system evolved as a behavioral system to promote infant's proximity to the caregiver

## What Are Attachment Behaviors?

- Result from a biological drive seen in all mammals and primates
- Describes the behavioral responses of a young child upon separation from his mother figure

## When Do We See Attachment Behaviors?

- Attachment system is activated when the infant is in a state of arousal (distress)
  - Absence/distance from caregiver
  - Caregiver departs
  - Unfamiliar situations
  - Illness
  - Hunger
  - Cold
  - Pain

Ainsworth, 1978

## Attachment Behaviors Promote Proximity

- Attachment behaviors are the infant's way of signaling the caregiver (protector) to come closer to the infant
  - Looking
  - Vocalizing
  - Crying/ Calling
  - Following
  - Clinging

⇒ Proximity Seeking and Contact Maintenance Behaviors

## Caregiver Responsiveness Influences Attachment Classification

Infant is distressed, signals caregiver

Caregiver responds consistently to signals

Infant learns that when he signals for his caregiver, his needs will be met

**SECURE** pattern of attachment results

## Caregiver Responsiveness Influences Attachment Classification

Infant is distressed, signals caregiver

Caregiver responds inconsistently to signals

Infant learns that when he signals for his caregiver, his needs will be not be met, or will be met inconsistently

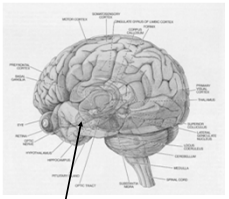
**INSECURE** pattern of attachment results

## Why Attachment Matters

- Early relationship experiences influence later child development
  - Patterns of the caregiver –child relationship as described by attachment theory have proven to be the most robust predictors of subsequent development. (Sroufe, 1988)
- Through the context of early relationships infant forms initial expectations about himself and others, which become internalized, and provide a framework for later social relationships
  - "Internal Working Model"

## Attachment and R Brain Development

- The quality of early experience impacts the experience-dependent maturation of the limbic system (Schore, 1994, 2001)
  - Secure attachment relationships facilitate synaptogenesis in R limbic system (Schore, 1994)
  - Mediates stress coping capacities of the individual
  - Early adverse attachment experiences result in brain organizations that are ineffective in regulating emotion and coping with stress. (Crittenden, 1988; Schore, 1997)

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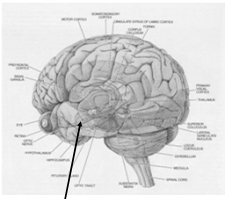


## Attachment and Child Development: Source of Resilience

- Secure attachment classification is related to
  - Increased social competence
  - Improved self-esteem
  - Persistence in problem solving
  - Increased independence
  - Decreased behavior problems
  - Increased resilience and protection against stress

(Sroufe, 1983; Sroufe, 1985, Pianta, 1990)

## Attachment and Child Development: Source of Vulnerability

- Insecure attachment classification is related to increased risk for later psychopathology
  - Boys with a history of avoidant or resistant attachment were more likely to be social withdrawn and have anxiety d/o (Lewis, 1984, Warren, 1997)
  - Early insecure attachment is associated with greater peer rejection and higher internalizing and externalizing behaviors in preschool (Wood, 2002, Guttman-Steinmetz, 2006)
- Early Disorganized infant-parent relationships affect later child development: (Carlson, 1998, Lyons-Ruth, 1996, Green, 2002)
  - More negative parent-child interactions
  - Increased child behavior problems in preschool, elementary school, HS
  - Increased aggression in school aged children
  - Later psychopathology and dissociation

## "Secure Attachment" Behaviors

- Actively seeks contact or interaction upon return
  - If distressed, seeks and maintains contact
  - If no distress, actively greets caregiver
  - Contact is effective in terminating distress
- Caregiver is a secure base for exploration
  - Readily separates to explore toys
  - Affective sharing of play
  - Readily comforted when distressed (returns to play)

Ainsworth, 1978

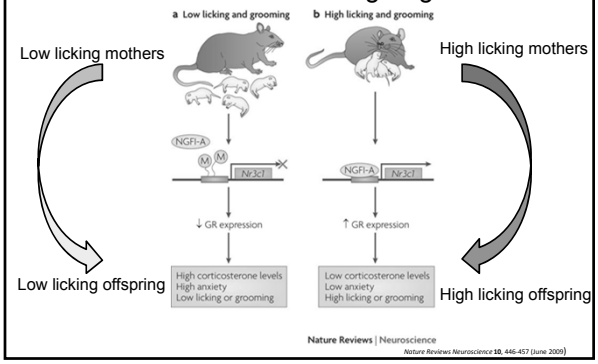
## Megan, 18 months

## Corrion, 25 months

## Promoting Resilience

NATURE **THROUGH** NURTURE

## The Neurobiology of Resilience:
### The Role of Caregiving

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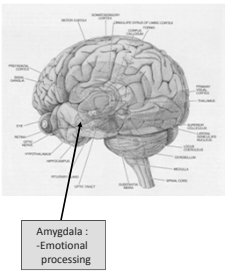



## The Neurobiology of Relationship
### Stress Reactivity of Children in Foster Care

- Salivary cortisol obtained from a sample of children in foster care and a comparison group
- Children in foster care demonstrated less decline in in levels across the day compared with non-foster care group
- *Conditions associated with foster care interfere with children's ability to regulate neuroendocrine functioning.*

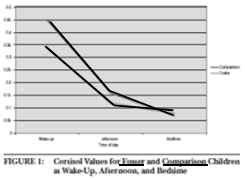


FIGURE 1: Cortisol Values for Foster and Comparison Children at Wake-Up, Afternoon, and Bedtime

CHILD MALTREATMENT, Vol. 11, No. 2, May 2006

## The Neurobiology of Relationship
### Stress Reactivity of Children After Intervention

- Relational intervention provided to children in foster care
- Cortisol reactivity was measured before and after stressor
- Cortisol reactivity in intervention group similar to non foster care group

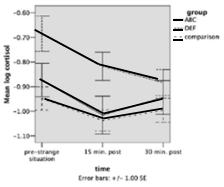


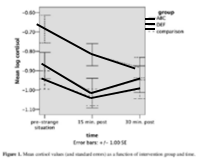

Figure 1. Mean cortisol values (and standard errors) as a function of intervention group and time.

***→ Improved stress reactivity with relational intervention***

*Development and Psychopathology* **20** (2008), 845–859

## Promoting Resilience in Foster Care:
## *Promoting Relationships*

- Intervention designed to help children in foster care develop regulatory capacity
- Intervention helps caregivers:
  1. Provide an environment to help child develop increased regulatory capacity
  2. Reinterpret child's alienating cues
  3. Provide consistent nurturing care

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## Promoting Resilience
### Intervention Goals

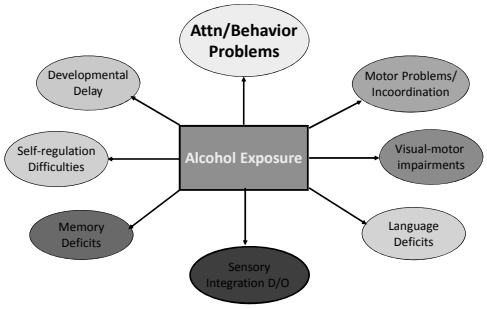
1. Provide an environment to help child develop increased regulatory capacity → STOP — Simplify and Structure Environment
2. Reinterpret child's alienating cues → SLOW — Respond Don't React
3. Provide consistent nurturing care → GO — Go Forth and Nurture

## Tools for the Toolbox

-Addressing Developmental needs
-Promoting First Relationships
-Handouts from the Circle of Security®

## Neurodevelopmental Consequences of Intrauterine Alcohol Exposure

*Infant –Toddler Symptoms*




TERATOLOGY 56:317–326 (1997)

## Diagnostic Workup

- Confirm / obtain history about prenatal alcohol exposure.

- Obtain comprehensive diagnostic evaluation to confirm diagnosis
  - Physical Exam
  - Assessment of Growth
  - Developmental/ Behavioral /Psychological assessment
  - Evaluate dysmorphology by a geneticist

- Provide developmental services to address areas of vulnerability

## Neurodevelopmental Consequences of Intrauterine Alcohol Exposure

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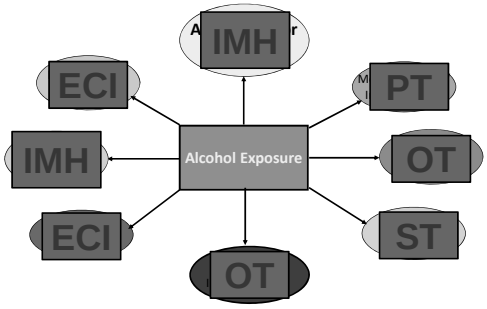
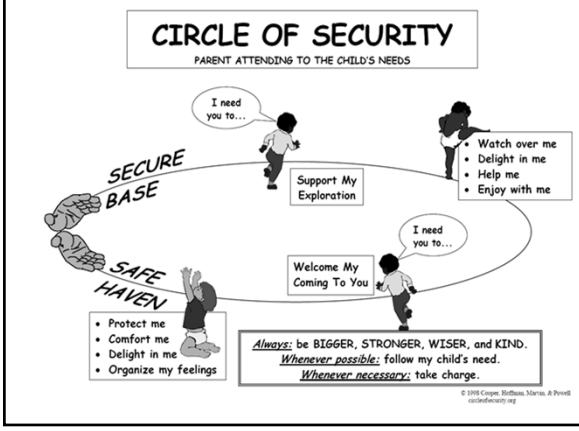
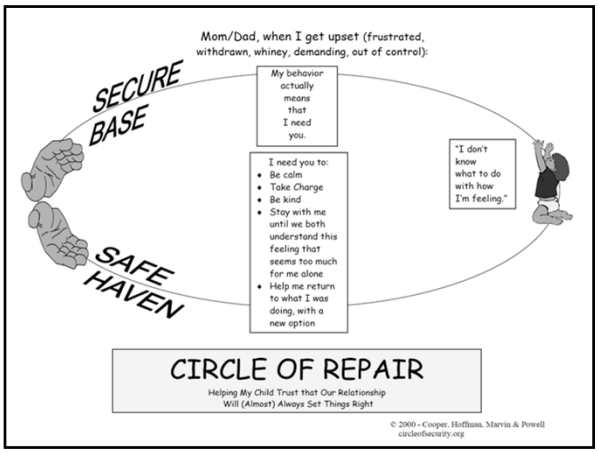


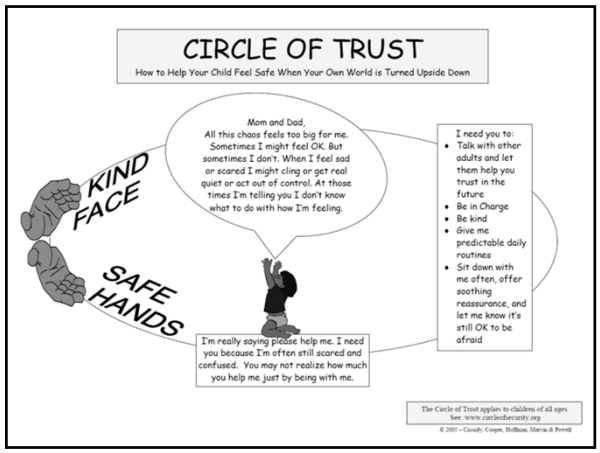

TERATOLOGY 56:317–326 (1997)

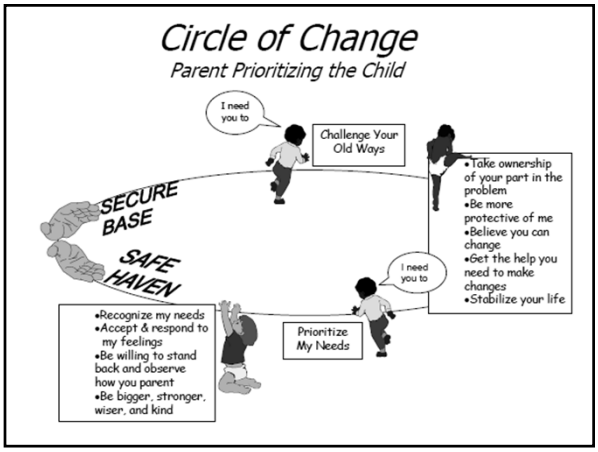
## Promoting First Relationships


**Dedicated to promoting children's social-emotional development through responsive and nurturing caregiver-child relationships**






## Promoting Resilience

Intervention Goals

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## (Almost) Everything I Need to Know About Being a Parent in 25 Words or less

***Always*: be BIGGER, STRONGER, WISER, and KIND.**

- ***Whenever possible*: follow your child's need.**
- ***Whenever necessary*: take charge.**

© Cooper, Hoffman, Marvin, & Powell – 1998 circleofsecurity.org

## What we hope for in parent-child relationships


**"This is my favorite place - inside your hug."**