Fetal Alcohol Spectrum Disorders

Desiree V. Rodgers, M.P.H., M.D., F.A.A.P.
Behavioral and Developmental Pediatrician
Diagnostic Center Central California

Fresno Diagnostic Center, Department of Education

Facts About Alcohol

- Effects of prenatal exposure to alcohol first described in the U.S. medical literature 30 years ago.
- 1968 Lemoine of Nantes, France, recognized the multiple effects that alcohol can have on the developing fetus (findings not well accepted).
- 1973 Jones et al. independently rediscovered the effects of alcohol on the developing fetus.

Smith's Recognizable Patterns of Human Malformation, 5th edition

Facts About Alcohol

- 1981—U.S. Surgeon General issued a public health warning that using alcohol during pregnancy could cause birth defects.
- 1989—Mandate established to label products containing alcohol.
- First International Fetal Alcohol Syndrome Awareness Day was observed on September 9, 1999.

Facts About Alcohol

- 2002--Congressional mandate that the CDC, the National Task Force on Fetal Alcohol Syndrome and Fetal Alcohol Effect, and other federally funded FAS programs, would develop guidelines for the diagnosis of FAS and other negative birth outcomes resulting from prenatal exposure to alcohol.
- September 9, 2004, observed as `National Fetal Alcohol Spectrum Disorders Day‘ in the U.S.

Incidence of Fetal Alcohol Spectrum Disorders (FASDs)

- Approximately 40,000 babies born per year with FASD's
- FASD's occur in all racial groups and across all socioeconomic strata
- Higher rates of FASDs in Native Americans and South Africans

FASD

- Definition of FASD:

  "FASD is an umbrella term describing the range of effects that can occur in an individual whose mother drank alcohol during pregnancy. These effects may include physical, mental, behavioral, and/or learning disabilities with possible lifelong implications. The term FASD is not intended for use as a clinical diagnosis."

National Task Force on Fetal alcohol Syndrome and Fetal alcohol Effect

FASD

- Many terms used to describe the continuum of effects resulting from prenatal exposure to alcohol:
  - -Fetal Alcohol Syndrome (FAS)
  - -Fetal Alcohol Effect (FAE)
  - -Alcohol-Related Birth Defects (ARBD)
  - -Alcohol-Related Neurodevelopmental Disorder (ARND)

Fetal Alcohol Syndrome (FAS)

- Institute of Medicine's 1996 Diagnostic Criteria for FAS:
  - -Confirmed maternal alcohol consumption (excessive drinking—regular, heavy, episodic)
  - -Characteristic facial features (short palpebral fissures, flat upper lip, flattened philtrum, flat midface)
  - -Growth retardation (decreased birth weight, failure to thrive postnatally not related to nutrition)

Fetal Alcohol Syndrome (FAS)

- Institute of Medicine's 1996 Diagnostic Criteria for FAS:

  -Central Nervous System (CNS) abnormalities (microcephaly, partial or complete absence of the corpus callosum, decreased size of cerebellum, neurosensory hearing loss, incoordination, impaired eye-hand coordination)

Partial Fetal Alcohol Exposure

- Confirmed maternal alcohol exposure
- Characteristic facial anomalies
- Either growth retardation, central nervous system neurodevelopmental findings, or other unexplained behavioral abnormalities

Alcohol Related Birth Defects (ARBD)

- Confirmed maternal exposure to alcohol
- Birth defects:

  -Cardiac (atrial septal defect, ventricular septal defect, Tetralogy of Fallot)

  -Skeletal (hypoplastic nails, shortened fifth digits, scoliosis, clinodactyly)

  -Renal (aplastic, dysplastic, hypoplastic kidneys, horseshoe kidneys)

Alcohol Related Birth Defects (ARBD)

- Birth Defects:

  -Ocular (strabismus, refractive problems secondary to small globes, retinal vascular anomalies)

  -Auditory (conductive hearing loss, neurosensory hearing loss)

Alcohol Related Neurodevelopmental Disorder (ARND)

- Confirmed maternal exposure to alcohol.
- Either central nervous system neurodevelopmental abnormalities or other unexplained behavioral abnormalities.

Alcohol Related Neurodevelopmental Disorder (ARND)

- Central nervous system neurodevelopmental findings:
  - -Microcephaly
  - -Structural brain abnormalities (agenesis of the corpus callosum, cerebellar hypoplasia, etc.)
  - -Other neurologic findings (fine motor difficulties, sensorineural hearing loss, poor gait coordination)

Alcohol Related Neurodevelopmental Disorder (ARND)

- Behavioral Abnormalities:
  - Poor school performance
  - Problems with social perception
  - Poor langauge abilities
  - Poor abstract reasoning
  - Learning Disabilities
  - Poor math skills
  - Impaired memory and judgment

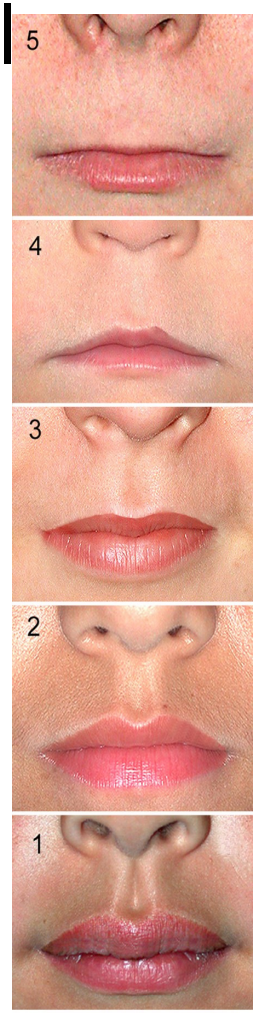
Pediatrics in Review Vol.22 No.2 February 2001

Weakness of Using IOM Criteria

- Normative values used for growth and facial features based on white populations
- Need to develop normal height and weight curves and anthropometric data for palpebral fissure lengths for other races
- Need formulation of lip/philtrum guides for various racial/ethnic groups

Diagnosing Fetal Alcohol Syndrome

- Prenatal maternal alcohol
- Growth deficiency
- Central nervous system abnormalities
- Dysmorphic features
  - Short palpebral fissures
  - Indistinct philtrum
  - Thin upper lip



Lip-Philtrum Guide 1

Caucasian

Lip-Philtrum Guide 2

African American

Source: Astley, S.J. 2004. *Diagnostic Guide for Fetal Alcohol Spectrum Disorders: The 4-Digit Diagnostic Code, Third Edition*. Seattle: University of Washington Publications Services, p. 114.

Risk Factors Associated with FASDs

- Dose of alcohol
- Pattern of exposure (binge vs. chronic)
- Developmental timing of exposure
- Genetic variation
- Maternal characteristics
- Socioeconomic status
- Synergistic reactions with other drugs
- Interaction with nutritional variables

Riley EP, McGee CL. Fetal alcohol Spectrum Disorders: an Overview with Emphasis on Changes in Brain and Behavior. Exp Bio Med 230:357-365, 2005.

Diagnosis of FASD

- Diagnosis made on prenatal history and physical features of child
- No laboratory or radiology studies available to make diagnosis
- Use multidisciplinary team approach to assist in making the diagnosis (physician, medical geneticist, psychologist, educational specialist)

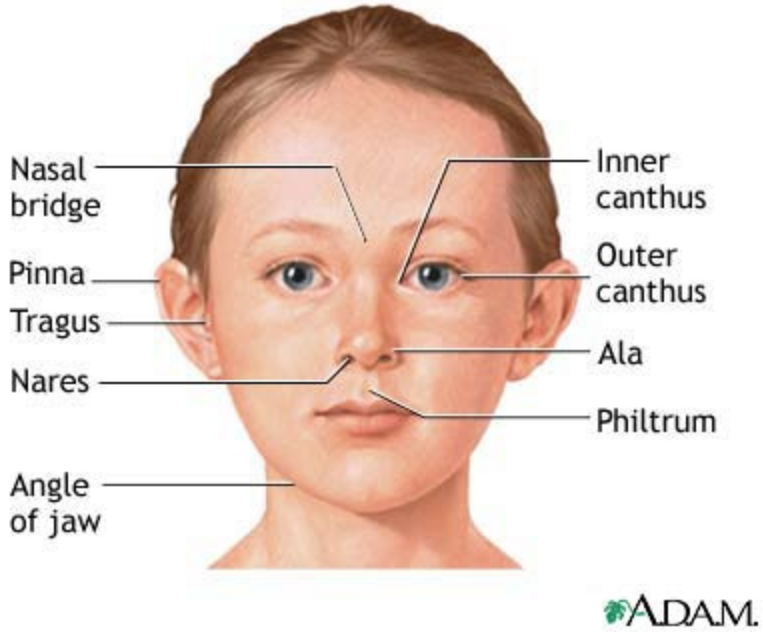
Differential Diagnosis of FASD

- Velocardiofacial syndrome (microdeletion of chromosome 22q11, short palpebral fissures, microcephaly, learning disabilities, broad nasal root with bulbous nasal tip, hypocalcemia, long slender fingers)
- Williams syndrome (microdeletion of chromosome 7qll mild prenatal growth deficiency, microcephaly, short palpebral fissures, long smooth philtrum, learning and behavioral problems, hypercalcemia, “cocktail party”personality, congenital heart defects)

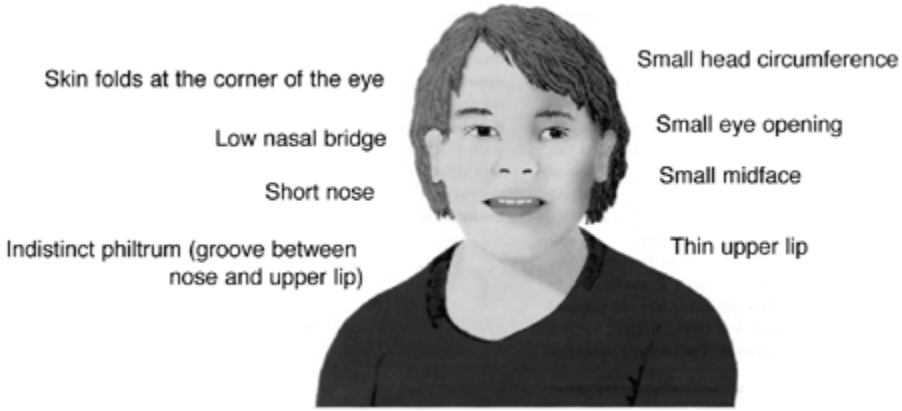
Differential Diagnosis of FASD

- Dubowitz syndrome (prenatal growth deficiency, mental retardation, microcephaly, short palpebral fissures, ptosis, exzema-like skin eruption, limb anomalies, cryptorchidism, ocular abnormalities)
- Cornelia de Lange syndrome (prenatal-onset growth deficiency, mental retardation, long philtrum, thin upper lip, synophrys, various limb defect most commonly micromelia)
- And many other genetic syndromes!!!

Identification of Normal Facial Features



Facial Features of Fetal Alcohol Syndrome



- Source: Warren, K.R., and Foudin, L.L. Alcohol-related birth defects—The past, present, and future. *Alcohol Research & Health* 25(3):153–158, 2001.

Comparison of a Child with Fetal Alcohol Syndrome with a Mouse Fetus Exposed to Alcohol in Utero on the 7th Day of Pregnancy

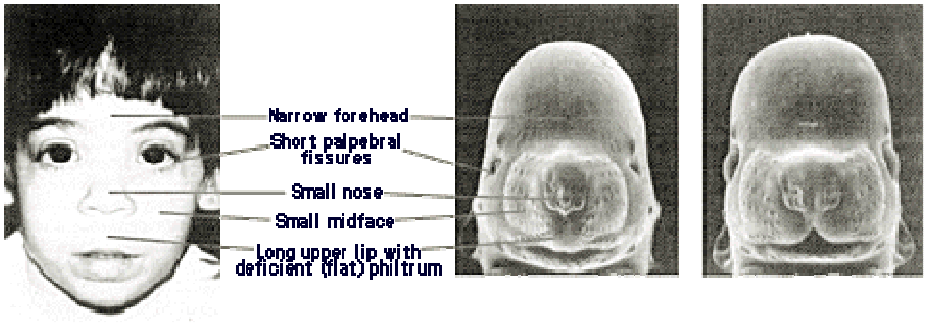


Photo courtesy of The University of North Carolina at Chapel Hill Bowles Center for Alcohol Studies

Fresno Diagnostic Center, Department of Education

Mouse Model of Intrauterine Alcohol Exposure

- 1980—Webster and colleagues showed that gestational stage-dependent abnormalities of the face and brain could be induced by alcohol in the offspring of C57BL6J mice
- Alcohol exposure on day 7 of pregnancy—exencephaly, mandibular hypoplasia, cyclopia, cleft lip
- Alcohol exposure on day 8 of pregnancy—maxillary hypoplasia associated with median cleft lip and cleft palate, occasional mandibular hypoplasia

Webster WS, Walsh DA, Pison AG, McEwen SE. Teratogenesis after acute alcohol exposure in inbred and outbred mice. Neurobehav Teratol 2:227-234, 1980.

Mouse Model of Intrauterine Alcohol Exposure

- 1981—Sulik and colleagues related the craniofacial malformations induced in mice at stages of embryogenesis that correspond to those occurring in Week 3 of human development
- Affected mouse fetuses had microcephaly, microphthalmia with short palpebral fissures, long upper lip with a deficient philtrum
- Facial deficiency related to involvement of median forebrain
- Forebrain deficiencies observed included hypoplasia or aplasia of the corpus callosum, hypoplasia of the basal ganglia, deficiency in the hippocampus, and the anterior cingulate cortex

Sulik KK, Johnston MC, Webb MA. Fetal alcohol syndrome: embryogenesis in a mouse model. Science 214:936, 1981.

Pathogenesis and Teratogenic Mechanisms of Alcohol

- Ethanol exposure leads to excessive cell death (apoptosis)
- Cell populations sensitive to ethanol-induced cell death:

  -anterior neural ridge (ANR)

  -neural crest cells

  -epibranchial placodes

  -subpopulations of the otic placodes or vesicles

Areas of the brain that can be damaged in utero by maternal alcohol consumption

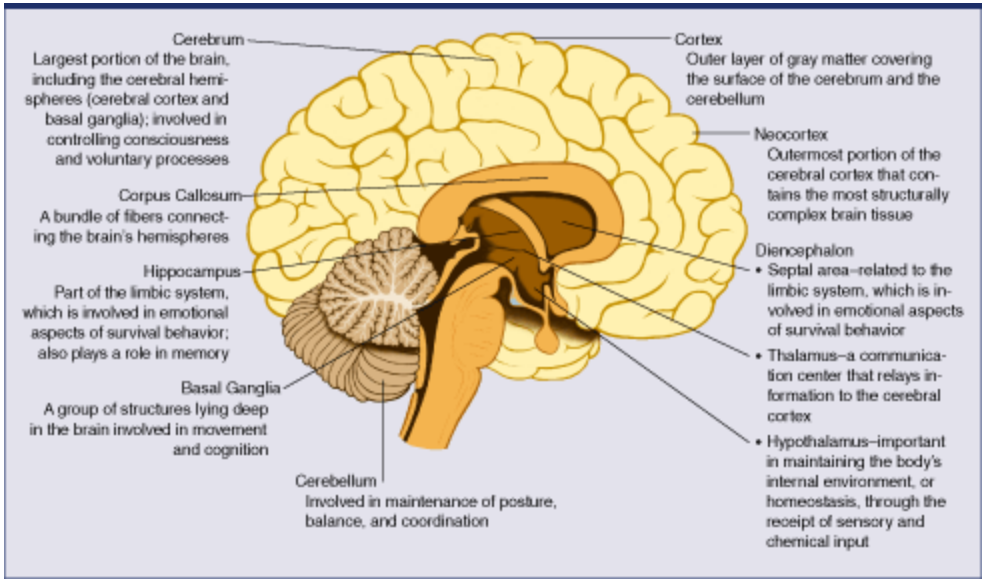
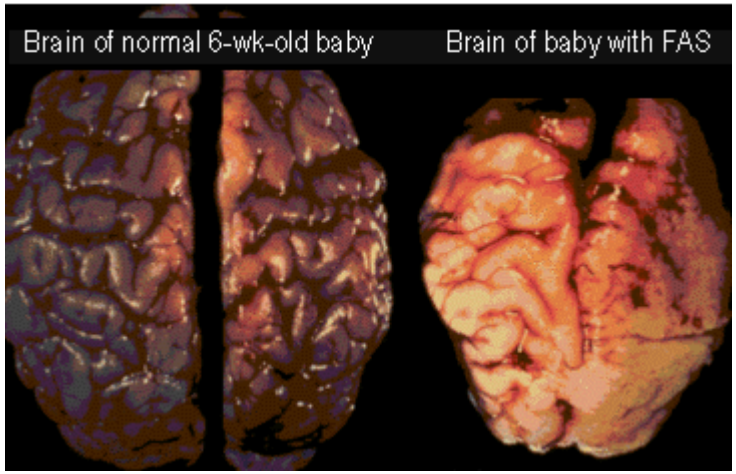


Photo courtesy of the National Institute on Alcohol Abuse and Alcoholism of the National Institutes of Health

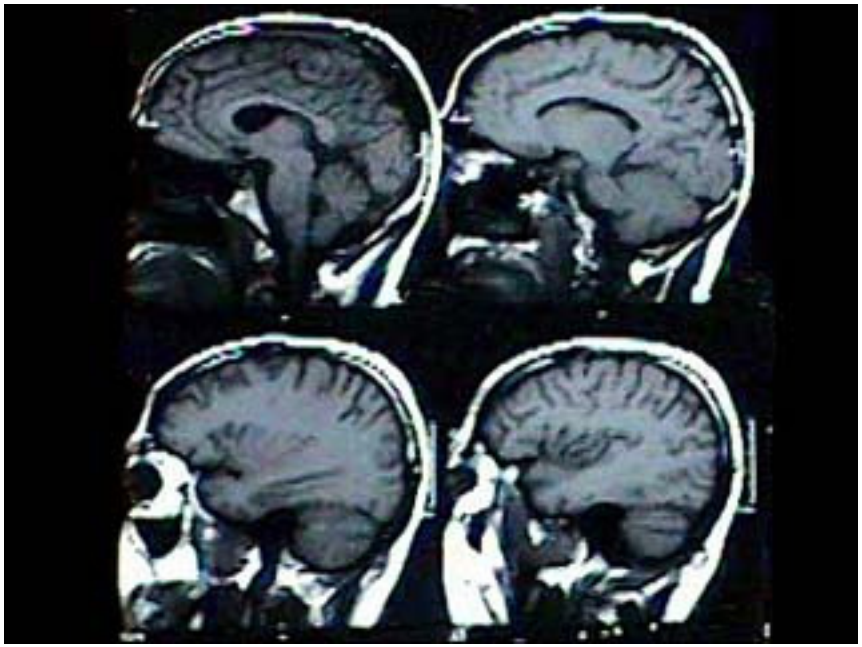
Fresno Diagnostic Center, Department of Education

Comparison of the brain of a normal 6 week old baby with the brain of an infant with FAS



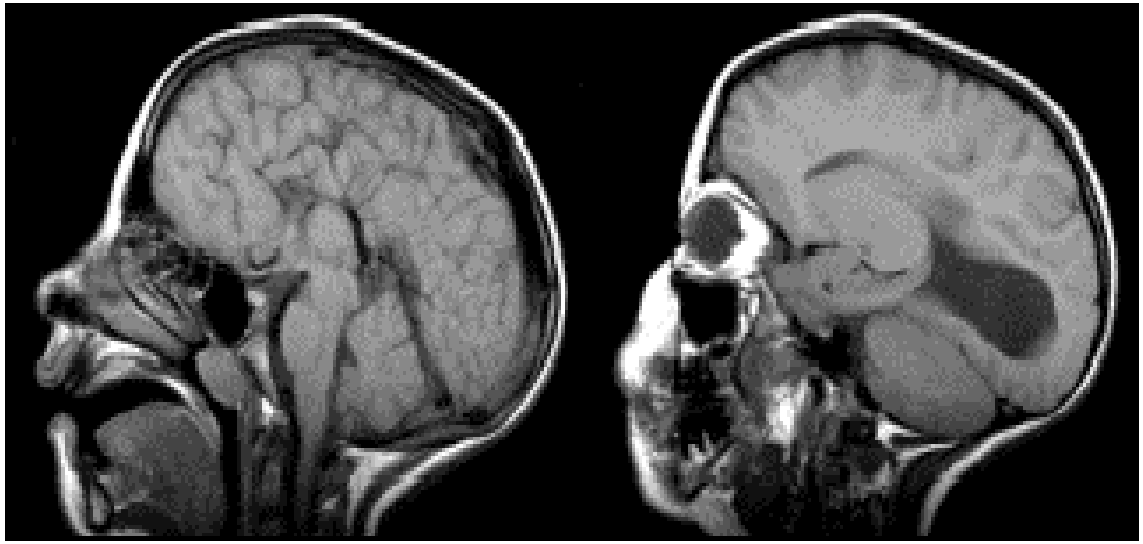
Fresno Diagnostic Center, Department of Education

MRI Scan of Human Brain



Fresno Diagnostic Center, Department of Education

FAS and the Brain



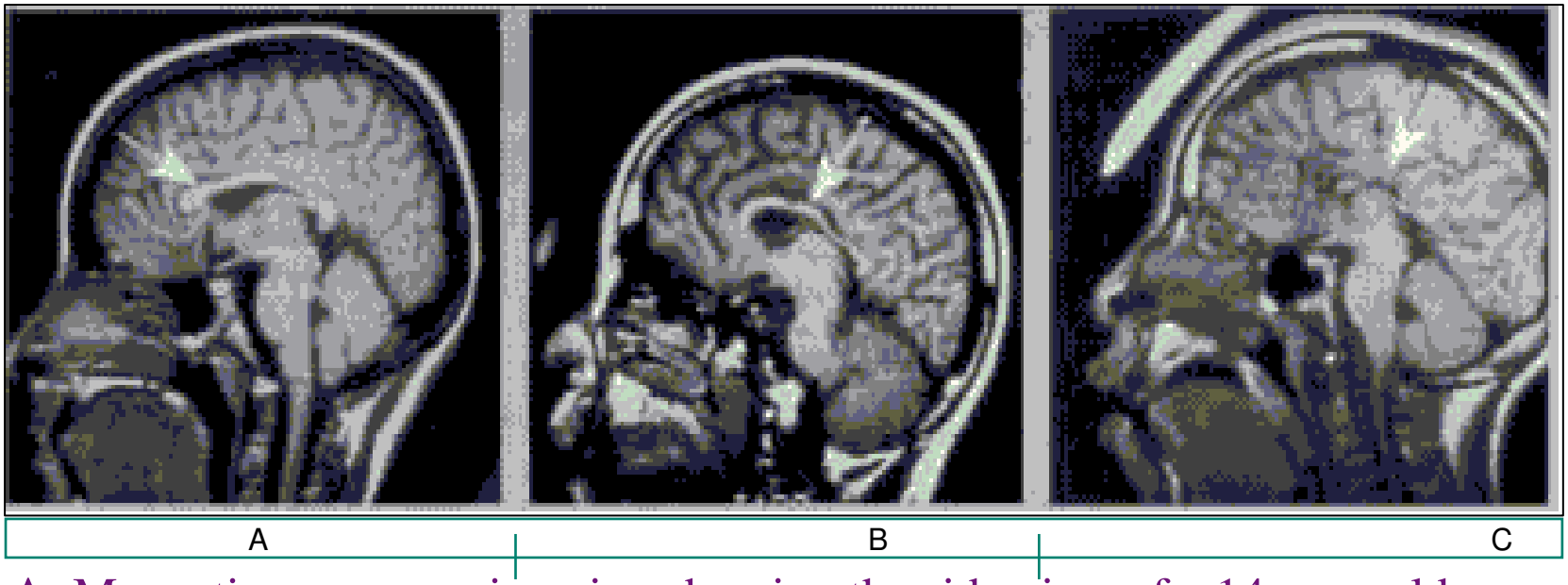
A

These two images are of the brain of a 9-year-old girl with FAS. She has agenesis of the corpus callosum, and the large dark area in the back of her brain above the cerebellum is essentially empty space.

Fresno Diagnostic Center, Department of Education

Source: Mattson, S.N., Jernigan, T.L., and Riley, E.P. 1994. MRI and prenatal alcohol exposure: Images provide insight into FAS. *Alcohol Health & Research World* 18(1):49–52.

FAS and the Brain



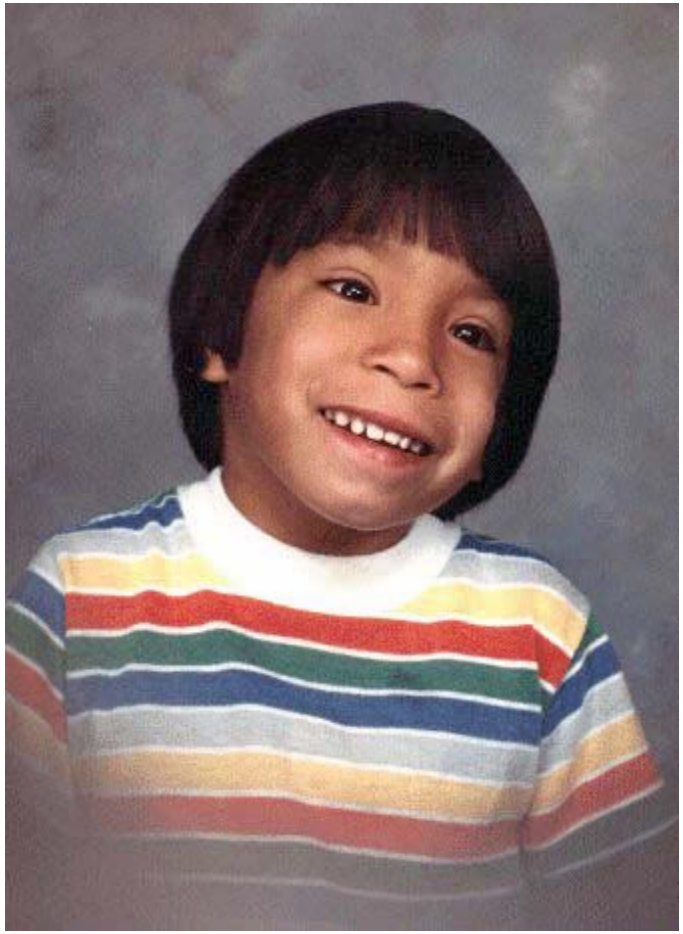
A. Magnetic resonance imaging showing the side view of a 14-year-old control subject with a normal corpus callosum; **B.** 12-year-old with FAS and a thin corpus callosum; **C.** 14-year-old with FAS and agenesis (absence due to abnormal development) of the corpus callosum.

Source: Mattson, S.N.; Jernigan, T.L.; and Riley, E.P. 1994. MRI and prenatal alcohol exposure: Images provide insight into FAS. *Alcohol Health & Research World* 18(1):49–52.

Fresno Diagnostic Center, Department of Education

Fresno Diagnostic Center, Department of Education

Fresno Diagnostic Center, Department of Education



Fresno Diagnostic Center, Department of Education

Fresno Diagnostic Center, Department of Education

Fresno Diagnostic Center, Department of Education

Cost of Fetal Alcohol Spectrum Disorders

- Actual cost unknown (expensive!!)
- Must factor in a child's
  - Educational needs
  - Medical needs (neurologist, cardiologist, ophthalmologist, etc.)
  - Dental needs
  - Supportive services (occupational therapy, physical therapy, speech and language therapy, etc.)
  - Additional support (regional center, SSI, etc.)

Summary

- No amount of alcohol is safe during pregnancy.
- The number of cases of FASDs outnumber the number of cases of FAS.
- Some children on the FASD will be missed due to lack of physical findings.
- There is no cure for FASDs.
- Early intervention is warranted.
- FASDs are 100% preventable.

FASD Resources

- National Organization on Fetal Alcohol Syndrome (www.nofas.org)
- California Fetal Alcohol Spectrum Organization (www.calfas.org)
- National Institute on Alcohol Abuse and Alcoholism (www.niaaa.nih.gov)
- National Clearinghouse for Alcohol and Drug Information (ncadi.samhsa.gov)
- SAMHSA FASD Center for Excellence (fasdcenter.samsha.gov)