Fetal Alcohol Syndrome

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DEPARTMENT OF COGNITIVE SCIENCE
UCSD
<table>
<thead>
<tr>
<th>Type of Defect</th>
<th>Characterized by</th>
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<tbody>
<tr>
<td>Developmental defect</td>
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<tr>
<td>Spina bifida</td>
<td>Paralysis below the level of the defect</td>
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<tr>
<td>Anencephaly</td>
<td>Failure in all major functions</td>
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<td>Genetic defect</td>
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<tr>
<td>Down syndrome</td>
<td>Altered facial features, decreased mental functioning, organ abnormalities</td>
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<tr>
<td>Phenylketonuria</td>
<td>If untreated, accumulation of phenylalanine and severe mental retardation</td>
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<tr>
<td>Fragile X syndrome</td>
<td>Abnormal facial features, mild to severe mental retardation</td>
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<td>Defect from external factors</td>
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<tr>
<td>Malnutrition</td>
<td>Decreased birth weight and increased mortality, low performance on tests of mental capacity</td>
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<tr>
<td>Fetal alcohol syndrome</td>
<td>Low birth weight, diminished height, distinctive facial features, hyperactivity and irritability, mental retardation</td>
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Failures of Neural Development: Environmental (external) factors

- **Fetal alcohol syndrome (FAS)**
  - **Cause**
    - Consumption of alcohol during pregnancy
  - **Characteristics**
    - Physical—diminished height, distinctive facial features, altered nose and eyelids
    - Behavioral and cognitive—mental retardation, hyperactivity, and irritability
Fetal Alcohol Syndrome:

Prevalence

The accurate prevalence of FAS and related conditions is not known. Several studies have found that the prevalence was 1 to 3 per 1,000 in live born infants. As noted above, the newborn period would not be the best time to identify all affected children. The facial characteristics may be harder to recognize, and the ability to determine the subtler forms of brain damage is poor or impossible at this age. It is likely that these studies of newborns undercounted the condition. The prevalence has been similarly calculated in populations that were judged to be high risk, and the reported rates of the disorder were much higher. About half of the individuals who have been diagnosed with FAS are reported to have mental retardation. As such, alcohol exposure is the most frequent known cause of mental retardation. This fact has been emphasized widely in the media. The fact that the other half of the population has serious cognitive processing deficits that do not readily qualify for services and societal understanding has not been well emphasized, however. The rates of brain damage in alcohol-exposed individuals who do not meet the diagnostic criteria for FAS may be several times higher than for FAS per se. It is not at all unreasonable to believe that as a conservative underestimate, ethanol has altered the brains of more than 0.5 to 1% of the American population as a whole.
Dr. Kenneth Lyons Jones Receives Lifetime Achievement Award In Genetics From March of Dimes

WHITE PLAINS, N.Y., MARCH 15, 2007 - Kenneth Lyons Jones, M.D., the renowned pediatrician and birth defects researcher who was one of two doctors who identified fetal alcohol syndrome (FAS), will receive the 2007 March of Dimes/Colonel Harland Sanders Award for lifetime achievement in genetic sciences.

The award will be presented to Dr. Jones on March 23 at the Annual Clinical Genetics Meeting of the American College of Medical Genetics in Nashville, Tennessee.

Dr. Jones is chief of the Division of Dysmorphology/Teratology in the Department of Pediatrics at the University of California, San Diego. He has been active in research, teaching, clinical work, and public service for nearly 40 years.

Dr. Jones' research has focused on dysmorphology, the study of birth defects, particularly those affecting the anatomy; identifying mechanisms of normal and abnormal fetal development; and recognition of new human teratogens (birth defects-causing agents). His book, "Smith's Recognizable Patterns of Human Malformation," is the reference used by health care professionals to diagnose and manage individuals with birth defects and genetic conditions.

Dr. Jones' most famous accomplishment is his coining of the term "fetal alcohol syndrome," with David W. Smith, M.D., to define the cluster of birth defects seen exclusively in the babies of women who used alcohol during pregnancy. In 1973, the two published their finding that alcohol was a teratogen in the British journal Lancet. That research was part of a March of Dimes-supported group focusing on diagnosis and treatment of birth defects.

He also established of the California Teratogen Information Service in 1979 to provide information to pregnant women and physicians about the potential teratogenic risk of drugs, chemicals and environmental agents to the developing fetus and to gain new information about their effects.

Dr. Jones is past president of the Western Society for Pediatric Research and the Teratology Society and co-chair of the Scientific Working Group on Diagnostic Guidelines for Fetal Alcohol Syndrome Disorder, convened by the National Center for Birth Defects & Developmental Disabilities at the Centers for Disease Control & Prevention.
The physical landmarks of the human face are very similar from one face to another.
A simian crease is a single palmar crease as compared to two creases in a normal palm. Simian crease occurs in about 1 out of 30 normal people, but is also frequently associated with other conditions such as Down syndrome, Aarskog syndrome or fetal alcohol syndrome.
Brain of baby with no exposure to alcohol

Brain of baby with heavy prenatal exposure to alcohol

Photo courtesy of Sterling Clarren, MD
SYMPOSIUM

Genesis of Alcohol-Induced Craniofacial Dysmorphism

Kathleen K. Sulik
Department of Cell and Developmental Biology and Bowles Center for Alcohol Studies,
The University of North Carolina, Chapel Hill, North Carolina 27599
A child with FAS (a) shares the typical craniofacial features, including microcephaly, short palpebral fissures, a small nose, and long (from nose to mouth) upper lip with a deficient philtrum, with a mouse fetus whose mother was treated with alcohol on her seventh day of pregnancy (b). Illustrated for comparison is a normal mouse fetus of the same developmental stage (c).
The face and forebrain of a normal gestational Day 11 mouse embryo (a and b) compared with those of three embryos (c and d; e and f; g and h) affected to differing degrees by maternal ethanol treatment on Day 7 of pregnancy illustrate concurrent loss of the “midline” tissues.

In particular, note the abnormally close proximity of the nostrils, with absence of portions of the medial nasal prominences (m), as well as similar abnormal proximity of the ganglionic eminences (g) and absence of the septal region (s).
Brain dysmorphology in individuals with severe prenatal alcohol exposure

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Our previous studies revealed abnormalities on structural MRI (sMRI) in small groups of children exposed to alcohol prenatally. Microcephaly, disproportionately reduced basal ganglia volume, and abnormalities of the cerebellar vermis and corpus callosum were demonstrated. The present study used sMRI to examine in detail the regional pattern of brain hypoplasia resulting from prenatal exposure to alcohol using a higher resolution imaging protocol and larger sample sizes than reported previously. Fourteen participants (mean 11.4 years; eight females, six males) with fetal alcohol syndrome (FAS) and 12 participants (mean 14.8 years; four females, eight males) with prenatal exposure to alcohol (PEA) but without the facial features of FAS were compared to a group of 41 control participants (mean 12.8 years, 20 females, 21 males). Findings of significant microcephaly and disproportionately reduced basal ganglia volumes in the FAS group were confirmed. Novel findings were that in FAS participants, white matter volumes were more affected than gray matter volumes in the cerebrum, and parietal lobes were more affected than temporal and occipital lobes. Among subcortical structures, in contrast to the disproportionate effects on caudate nucleus, the hippocampus was relatively preserved in FAS participants. Differences between the PEA group and controls were generally non-significant; however, among a few of the structures most affected in FAS participants, there was some evidence for volume reduction in PEA participants as well, specifically in basal ganglia and the parietal lobe. There were no group differences in cerebral volume asymmetries. Severe prenatal alcohol exposure appears to produce a specific pattern of brain hypoplasia.
Brain abnormalities

- Acallosal – agenesis of the corpus callosum
- Thin corpus callosum - disgenesis

Normal child

FAS children with focally thin Corpus callosum or acallosal.

(Mattson, Jernigan, & Riley, 1994).