Lesson S28: PreAnesthetic Assessment of the Child with Fetal Alcohol Syndrome

Authored by: Elizabeth A.M. Frost MD, Clinical Professor of Anesthesia, Mount Sinai School of Medicine, New York, NY

Reviewed by: Ram Roth MD, Assistant Professor, Mount Sinai School of Medicine, New York, NY

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Read this article, reflect on the information presented, then go online and complete the lesson post-test and course evaluation before the termination date below. (CME credit is not valid past this date.) You must achieve a score of 80% or better to earn CME credit.

TIME TO COMPLETE ACTIVITY: 2 hours
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Practice Gaps

Excessive alcohol consumption remains a prevalent societal problem. Fetal alcohol spectrum disorders (FASD) are a common cause of intellectual impairment and birth defects. A simple search of the medical literature easily retrieves more than 4,000 publications addressing fetal alcohol syndrome. Anesthesiologists should have knowledge of the classic presentation of a newborn affected by maternal alcohol consumption, as well as the effects of alcohol on the child and the perianesthetic considerations.

Objectives

At the end of the lesson, the participant will be able to:

1. List the most common abnormalities in the newborn of an alcoholic mother
2. Describe maternal factors that contribute to alcohol intake.
3. Cite federal legislation about alcohol consumption during pregnancy
4. Identify the critical period for alcohol teratogenicity
5. Recognize the effects of acetaldehyde on the fetus
6. Identify biochemical markers that may be used to predict FASD
7. List chromosomal abnormalities that have been associated with maternal alcohol intake
8. Prescribe an anesthetic plan for a child with FASD
9. State the prevalence rate for FASD in the United States
10. Offer a brief historical account of fetal alcohol syndrome

Case Presentation

A 3 year old female child was scheduled for correction of strabismus. The child lived in a State-administered facility as she was abandoned by her mother who was reportedly homeless with an alcohol abuse problem. Her birth was recorded at 35 weeks gestation. Upon examination, the child
weighed 18 lbs and preferred crawling to walking. She was microcephalic and had a hypoplastic mandible. She was receiving seizure medications with the last recorded seizure event 3 months prior.

**Introduction**

Alcohol consumption exerts profound and often devastating effects on both the parturient and the fetus. *Fetal alcohol spectrum disorder* (FASD) includes fetal alcohol syndrome (FAS) and other conditions resulting from prenatal alcohol exposure. The International Statistical Classification of Diseases and Related Health Problems and assigned ICD-9 diagnoses only recognize FAS as an outcome of prenatal alcohol exposure. Children born to women who consumed excessive amounts of alcohol during pregnancy have cardiovascular, craniofacial, and limb defects that are typically associated with prenatal growth deficiency and developmental delay. Chronic alcoholism is frequently associated with drug abuse and it may be difficult to implicate ethanol as the single cause of defects. Studies have shown that animal fetuses exposed to excessive ethyl alcohol develop dysmorphic features similar to those seen in exposed human fetuses.

**Historical references**

There is a well-documented historical awareness of the link between maternal alcohol use and negative child outcomes as evidenced by anecdotal accounts of prohibitions against maternal alcohol use in biblical, ancient Greek, and ancient Roman sources. In early laws throughout Scotland, the mother and nurse were restricted from consuming any amount of “ale” during pregnancy, or during the period of breastfeeding.

A link between maternal alcohol use and fetal damage was noted in 1899 by Dr. William Sullivan, a Liverpool prison physician who recorded higher rates of stillbirth for 120 alcoholic female prisoners as compared to sober female relatives. Sullivan suggested the causal agent to be alcohol use. His observation contradicted the common belief that heredity alone was the cause of mental retardation, poverty, and criminal behavior. A case study described by Goddard of a family (the Kallikak family) supported this position which was in line with discussions on alcoholism throughout the mid-1900s. Researchers later suggested that the Kallikak family almost certainly had FAS.

Prior to FAS being specifically defined and named in 1973, a few published studies noted differences between the children of mothers who used alcohol during pregnancy or breast-feeding and those who did not; and identified alcohol use as the possible contributing factor rather than heredity. Dr. Paul Lemoine published a study in a French medical journal in 1968 about children with distinctive features born to alcoholic mothers. Ulleland and colleagues at the University of Washington Medical School conducted an 18-month study in 1968–1969 documenting the risk of maternal alcohol consumption among the offspring of 11 alcoholic mothers. The findings of these two studies were confirmed by Olegrad et al in Sweden. The children in all three studies were similar in appearance and behaved in a similar unfocused and hyperactive manner.

The term “fetal alcohol syndrome” was coined in 1973 by Jones and Smith, two pediatricians at the University of Washington Medical School. They identified the pattern of craniofacial, limb, and cardiovascular defects in eight unrelated children born to alcoholic mothers in three ethnic groups. The pattern of malformations indicated that the damage was prenatal.
In the years following Jones and Smith’s categorization of the syndrome, the Dysmorphology Unit at the University of Washington diagnosed 41 patients with FAS. In 1976, the Unit evaluated 65 patients. A German study described 85 patients with FAS - and more than 100 cases were reported elsewhere.

The University of Washington Primate Center carried out animal studies and confirmed that alcohol was a teratogen. By 1978, 245 cases of FAS had been reported by medical researchers, and the syndrome was described as the most frequent known cause of mental retardation.

As subsequent research and clinical experience suggested that a range of effects (including physical, behavioral, and cognitive) could arise from prenatal alcohol exposure, the term Fetal Alcohol Spectrum Disorder (FASD) was adopted to include not only FAS but also fetal alcohol effects (FAE), partial fetal alcohol syndrome (PFAS), alcohol related birth defects (ARBD) and alcohol related neurodevelopmental disorder (ARDD).

**Incidence**

Alcohol use is widespread. In 1988, the US government issued the Alcoholic Beverage Labeling Act requiring that warning labels be placed on all alcoholic beverage containers with the message that “women should not drink alcoholic beverages during pregnancy because of the risk of birth defects”. In 2005, the Surgeon General issued a health advisory encouraging women to abstain from alcohol use while pregnant or while planning a pregnancy.

Fetal alcohol exposure is the leading known, non-genetic cause of mental retardation in Western world cultures. In the United States, the prevalence rate of FAS is estimated to be between 0.2 and 2.0 cases per 1,000 live births, comparable to or higher than most other developmental disabilities such as Down syndrome or spina bifida. Annually, approximately 80,000 pregnant women consume alcohol through all 3 trimesters of pregnancy. Cigarette smoking and delayed prenatal care are often associated with alcohol consumption. The lifetime medical and social costs of each child with FAS may be as high as one million US dollars.

There has been controversy regarding whether or not there is a safe level of alcohol consumption during pregnancy. Several studies indicate that light to moderate drinking during pregnancy might not pose a risk to the fetus, although no amount of alcohol during pregnancy can be guaranteed to be absolutely safe. The Royal College of Obstetricians and Gynaecologists in the United Kingdom conducted a study of over 400,000 women who consumed alcohol during pregnancy. No case of fetal alcohol syndrome occurred and no adverse effects on children were found when consumption was under 8.5 drinks per week. Other studies found that FAS only occurred among alcoholics; no apparent risk to the child occurred when the pregnant women consumed no more than one drink per day. Forrest and du Florey studied moderate drinking during pregnancy and found no negative effects. The researchers concluded that one drink per day provides a significant margin of safety, although they did not encourage drinking during pregnancy. Du Florey reported the findings of another study of pregnancies in eight European countries which found that consuming no more than one drink per day did not appear to have any effect on fetal growth. A follow-up of these children at 18 months of age found that those children from women who consumed alcohol during pregnancy, even two drinks per day, scored higher in several areas of development. An analysis of seven medical research studies involving over 130,000 pregnancies found that consuming two to 14 drinks per week did not increase the risk of giving birth to a child with either malformations or fetal alcohol syndrome.
Hanson et al found that during early pregnancy, even moderate amounts of alcohol could adversely affect the fetus. Mills and Graubard reported a trend in abnormalities but no increases in total malformations among moderate drinkers.

Painter et al noted that siblings born from an alcoholic mother may vary in severity of FAS symptoms. Furthermore, one twin may have few anomalies while the other is grossly deformed.

Burd et al linked prenatal alcohol exposure to increased risk of fetal mortality, stillbirth and infant and child mortality. The researchers noted that 1-2 hours after maternal ingestion, fetal blood alcohol concentrations reach levels nearly equivalent to maternal levels. A fetus has prolonged exposure to alcohol because metabolic capacity is insufficient and ethanol elimination is delayed. Moreover, there is reuptake from the amniotic fluid by the fetus. Alcohol elimination relies on maternal metabolic capacity which was found to vary as much as eight fold among pregnant women, which may explain the widely varying phenotypic presentations of FASD.

In a study of more than 79,000 mothers enrolled in the Danish National Birth Cohort in 1996-2002, infant mortality in the first year was 279 children. Mortality in the immediate neonatal period (204 children) was not associated with alcohol consumption of 4+ drinks/week or binge drinking on 3+ occasions. However, an association with alcohol intake and those who died in the post neonatal period was made.

Pathophysiology

The critical period for alcohol-induced teratogenicity appears to be around the time of conception. Multiple chromosomal anomalies have been demonstrated in fetal mice when the mothers were fed alcohol prior to and during pregnancy. Isochromosome 9q abnormality resulting in trisomy 9q and monosomy 9q has been described. Trisomy 21 may also be associated with FAS.

Acetaldehyde may cause fetal damage. The cotyledon of the placenta oxidizes ethanol to acetaldehyde, releasing it to the fetal perfusate. Acetaldehyde is transferred to the fetal side of the placenta, reaching 50% of the maternal level. Also, 95% of maternal alcohol is metabolized in the liver as acetone. Conversions of alcohol and acetaldehyde produce excess adenine dehydrogenase which may cause many of the metabolic abnormalities associated with alcohol abuse (e.g. hyperlactacidemia). During the first trimester, the effects of high concentrations of acetaldehyde on cell membrane and migration may alter embryonic organization of tissue resulting in dysmorphic changes. Growth retardation may also be linked to the ability of alcohol to interfere with the passage of amino acids across the placenta and the incorporation of amino acids into proteins, which may limit the number of fetal cells. Histologic studies of the brain of infants exposed to alcohol in utero demonstrate structural changes due to failure or interruption of neuronal and glial migrations. Consistent anomalies include cerebellar dysplasias and heterotopic cell clusters. Malformations of the cerebrum appear to be associated with microcephaly and subventricular malformations with hydrocephaly. Other studies have shown inhibition of glutamate receptor-mediated synaptic plasticity (e.g. N-methyl-d-aspartate-dependent long term potentiation) by alcohol. The effect of ethanol on glutamate may well play a role in causing abnormalities in the developing brain.

Low levels of alpha-fetoprotein and pregnancy-specific beta 1 glycoprotein have also been used to predict FAS in > 50% of cases and may prove to be useful biochemical markers.
The incidence of spontaneous abortion in women who drink to excess is increased and approximately 40-50% deliver prematurely. FAS is also associated with breech presentations but confounding factors include poor prenatal care and other substance ingestion as noted above.

**Signs and Symptoms of FAS**

The diagnostic criteria for FAS are shown in Table 1. Associated factors include increased rates of mental retardation, seizure disorders, brain malformations and premature mortality. Impaired motion perception may be indicative of a dorsal stream development dysfunction.34

<table>
<thead>
<tr>
<th>Growth and Performance</th>
<th>Craniofacial</th>
<th>Limb</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prenatal growth deficiency</td>
<td>Short palpebral fissures</td>
<td>Abnormal palmar creases</td>
<td>Cardiac defects (septal defects)</td>
</tr>
<tr>
<td>Postnatal growth deficiency</td>
<td>Midfacial hypoplasia</td>
<td>Joint anomalies</td>
<td>External genital and ear anomalies</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>Epicanthic folds</td>
<td>Hyperactivity</td>
<td>Hemangiomas</td>
</tr>
<tr>
<td>Developmental delay or mental retardation</td>
<td>Seizures</td>
<td>Hip dislocation</td>
<td>Immune dysfunction</td>
</tr>
<tr>
<td>Fine motor dysfunction</td>
<td>Visual disturbances</td>
<td>Poly and syndactyly</td>
<td>Sleep disturbance</td>
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The presentation of growth retardation, major and minor anomalies, central nervous system involvement and facial dysmorphology may also be seen in the fetal hydantoin syndrome (born to mothers on anti-epileptic medication). The diagnosis of FAS is usually made either in utero (small head circumference) or in the newborn but may be delayed for months. One confounding factor may be the effects of alcohol withdrawal after delivery; some infants may show irritability, tremors, seizures, opisthotonus and abdominal distension; a picture similar to that induced in animals withdrawn from ethanol or in neonates born to narcotic addicts.

Birth weight tends to be low, although gestational age may approach normal. Postnataally, babies do not demonstrate “catch-up”. Decrease of adipose tissue is a consistent feature.31 Mental retardation is one of the most common features of FAS. The average IQ of these children is about 70-89 and at least 85% score > two deviations below the mean.31 Questions have been raised as to whether low IQ is related to exposure to ethanol in utero or a result of being raised by an alcoholic mother. In utero damage is more plausible as there is a strong correlation between dysmorphism and lower IQ which exists in those children raised in stable foster homes and those raised by addicted parents. Distortion in facial appearance is most obvious. Facial image analysis has recently been developed for delineation of the facial phenotype associated with the FASD.37 The main features are outlined in Table 2.
Table 2: Facial characteristics of Fetal Alcohol Syndrome

<table>
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<tr>
<th>Eyes</th>
<th>Ears</th>
<th>Cheeks</th>
<th>Mouth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short palpebral fissures</td>
<td>Low set</td>
<td>Hypoplastic maxillae</td>
<td>Hypoplastic upper lip</td>
</tr>
<tr>
<td>Epicanthic folds</td>
<td>Posterior rotation</td>
<td></td>
<td>Thinned vermilion</td>
</tr>
<tr>
<td>Strabismus, myopia</td>
<td>Abnormal concha</td>
<td></td>
<td>Micrognathia</td>
</tr>
<tr>
<td>Ptosis, nystagmus</td>
<td>Poorly formed pinnae</td>
<td></td>
<td>High arched or cleft palate</td>
</tr>
<tr>
<td>Glaucoma</td>
<td></td>
<td></td>
<td>Abnormal dentition</td>
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Up to 90% of affected infants have abnormalities of the eye of which there are two kinds: hypoplasia of the optic nerve head (up to 48%) and increased tortuosity of the retinal vessels, especially the arteries (up to 49%). Visual acuity is severely decreased.

Cardiac lesions are detected in approximately 40% of infants consisting mostly of ventricular septal defects although tetralogy of Fallot and atrial septal defects have also been described. Pulmonary hypertension and unilateral pulmonary artery stenosis are other associated defects.

A study of 23,573 live births reported from Australia found 292 cases of cerebral palsy. The odds of heavy alcohol intake in the mothers was an adjusted odds ratio of 3.32 (95% confidence interval equal to 1.30-8.48). Both prenatal and perinatal acquired cerebral palsy was associated with alcohol consumption.

Anesthetic Management

The presence of mental retardation will decrease the likelihood that the child with FASD will be cooperative. In addition, the child may be deaf and/or blind with cardiac problems. Table 3 presents the major anesthetic concerns when working with a child with FASD. Considerations generally involve the selection of appropriate drug dosages, maintenance of normothermia and vigilance to prevent post-anesthetic apnea.

Table 3: Several factors to be considered in the anesthetic management of the child with FASD

<table>
<thead>
<tr>
<th>Anesthetic Considerations of Fetal Alcohol Syndrome</th>
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<tbody>
<tr>
<td>Prematurity</td>
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<tr>
<td>Mental retardation</td>
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<tr>
<td>Cardiac involvement</td>
</tr>
<tr>
<td>Drug interaction</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
</tr>
<tr>
<td>CNS involvement</td>
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<tr>
<td>Difficult airway</td>
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</tbody>
</table>

As most FAS babies receive anti-seizure medication, the risk of drug interactions exists. Assessment of renal and hepatic function should be made as many anesthetic agents depend on these organs for elimination. FAS children are rarely candidates for outpatient and ambulatory care.
Treatment

There is no cure for FASD because damage to the CNS damage creates a permanent disability. CNS damage, symptoms, secondary disabilities, and needs vary widely by individual. Treatment largely addresses symptoms and is commensurate with the degree of abnormality. Comprehensive, multi-model approaches based on the needs of the patient are most successful. Several treatment models have been identified, but regardless of the predominant approach, multiple types of interventions are incorporated to ameliorate the negative effects.

FASD is now recognized as the leading cause of non-genetic retardation in the United States (about 1 in 500 births). The primary mode of prevention is abstinence from alcohol during pregnancy. Detection, diagnosis and treatment remain a serious public health need. Developmental anomalies are a result of distortion of the biochemical molecules involved in signal transduction and synaptic pathways, consisting primarily of transmitters and neurotrophic peptides. Recent advances include the use of small molecule agonists, antagonists and competitive inhibitors to ameliorate symptoms. Biomarkers for FASD have been identified and multicenter screening feasibility studies are warranted. In vitro studies have shown that metformin and thymoquinone are strong protective agents against ethanol-induced neuronal apoptosis in rat cortical neurons. These agents may have the potential to buffer ethanol toxicity during early brain development.

Studies among women in South Africa, which has the highest incidence of FASD worldwide, have raised important issues of prediction and prevention. Factors contributing to FASD were found to be low maternal weight, smoking, early onset of drinking, a male partner who also drank, unmarried state and poor socio-economic status. Education, awareness of FASD, and restriction in alcohol use were shown to be possible and successful approaches in reducing the problem.

Management of the Case

In the case presented, examination of the airway revealed a possible difficult intubation. In view of this, all materials necessary to perform an intubation were available including a variety of tubes and supraglottic devices. After a smooth inhalation induction with sevoflurane during which time, ventilation was easy, an unsuccessful attempt was made to visualize the larynx. The smallest laryngeal mask airway was placed without difficulty. Oxygenation was well maintained and capnography showed an excellent waveform. Surgery was completed in 35 minutes. Although the child awoke quickly, she was very agitated and a decision was made to observe her overnight. She was discharged the following day.
References

18. Wilkie S. Global overview of drinking recommendations and guidelines. *AIM Digest* (Supplement), June 1997, 2–4, p. 4
POST-TEST

1. The incidence of FASD in the United States is:
   a. Largely unknown
   b. About 1 case per 1,000 live births
   c. Increasing every year at an alarming rate
   d. So rare that estimates are not available

2. Babies born to alcoholic mothers are:
   a. Often premature
   b. Attain normal weights quickly
   c. Usually overweight
   d. Very similar to babies born of non-alcoholic mothers

3. Consuming one drink per day:
   a. Results in reproducible fetal and neonatal defects
   b. Is advocated by the US Surgeon General
   c. May not have any demonstrable effect on the fetus
   d. Decreases the incidence of maternal complications

4. Historical notes regarding FAS indicate:
   a. It was described in Biblical times
   b. A link between alcohol and fetal damage was made prior to 1900
   c. Identification as a syndrome was made about 40 years ago
   d. All of the above

5. The least likely associated feature of FASD is:
   a. Mental retardation
   b. Strabismus
   c. Atonia
   d. Seizures
6. **Regarding cardiac lesions in FASD:**
   a. They occur in about 80% of FASD babies
   b. The most common is ventricular septal defect
   c. Fallot of tetralogy is never seen
   d. They represent the most common cause of neonatal death

7. **Fetal effects of alcohol are least likely related to:**
   a. Prolonged exposure because of insufficient metabolic capacity
   b. Production of excessive amounts of adenine dehydrogenase
   c. Fetal reuptake of alcohol from the amniotic fluid
   d. Low concentrations of acetaldehyde resulting in a build-up of damaged cells

8. **Biochemical markers of FASD include:**
   a. High levels of alpha-fetoprotein
   b. Low levels of specific beta 1 glycoprotein
   c. Increased glutamate receptor-mediated synaptic plasticity
   d. Decreased levels of amniotic acetaldehyde

9. **Anesthetic considerations for the child with FASD include:**
   a. Inability to cooperate
   b. Difficult airway
   c. Drug interactions
   d. All of the above

10. **Regarding treatment for FASD:**
    a. Multi-modal approaches based on patient needs are most successful
    b. In vivo studies suggest that metformin reduces apoptosis
    c. Anti-seizure medications have no effect
    d. None is required as the syndrome improves greatly with age