Fetal Alcohol Spectrum Disorder

Robert J. Sokol, MD
Virginia Delaney-Black, MD, MPH
Beth Nordstrom, PhD

FETAL ALCOHOL SYNDROME (FAS), currently considered part of fetal alcohol spectrum disorder (FASD), was first described in 1973.[1] Although much has been learned in 30 years, substantial challenges remain in diagnosing and preventing this disorder. Our goal is to summarize what has recently been reported with respect to fetal alcohol terminology, identification, effects, prevalence, and prevention of exposure. We will emphasize how fetal alcohol exposure is routinely underidentified and what is known about who is at risk. With this knowledge, physicians should be better able to identify at-risk pregnancies and alcohol-affected individuals and address fetal alcohol exposure in the clinical setting.

Fetal Alcohol Terminology

Fetal alcohol syndrome is diagnosed when characteristic facial dysmorphology, growth restriction, and central nervous system/neurodevelopmental abnormalities are present, with or without confirmed prenatal alcohol exposure.[2] Although it has long been recognized that affected individuals may have some but not all of the FAS characteristics, research has not identified a reliable way of defining those individuals who are less affected. Fetal alcohol effects (FAE), prenatal alcohol effects (PAE), alcohol-related birth defects (ARBD), and alcohol-related neurodevelopmental disorder (ARND) have all previously been suggested as terms to identify those children with a spectrum of problems but not classic FAS.

Although much available research still uses the older nomenclatures, the term FASD has recently been used by advocates, educators, and federal agencies (National Institute on Alcohol Abuse and Alcoholism and Centers for Disease Control and Prevention) as an umbrella term to cover the range of outcomes associated with all levels of prenatal alcohol exposure. Adoption of a common and overarching term, such as FASD, will allow researchers and physicians who work with affected individuals to better understand and describe the current state of knowledge.

Identification of Drinking During Pregnancy

How much drinking during pregnancy is too much? For nonpregnant women, physicians and many researchers define light drinking as 1.2 drinks per day, moderate drinking as 2.2 drinks per day, and heavy drinking as 3.5 or more drinks per day.[3] However, risk-drinking during pregnancy (enough to potentially damage offspring) has been defined as an average of more than 1 drink (0.5 oz) per day,[4] or less if massed (binges of >5 drinks per episode). Although many reports of adverse effects related to prenatal exposure involve heavier drinking,[5-7] recent research documenting deleterious outcomes for children prenatally exposed to small amounts of alcohol (0.5 drink per day)[8] has led to recognition that a threshold has not been adequately identified. This, along with varying susceptibility (vulnerability), leads to the conclusion and recommendations by both the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists that abstinence during pregnancy should be recommended to preconceptional and pregnant women.

Detection of maternal alcohol exposure is a particular challenge; no reliable biological marker is available. Although analysis of both meconium and hair samples for fatty acid ethyl esters has been proposed, there are no large population-based validation studies for these methods.[9] Similarly, other biochemical markers, including γ-glutamyl transferase, hemoglobin-associated acetaldehyde, and carbohydrate-deficit transferrin, have not yet been validated or have not been shown to have adequate diagnostic sensitivity and specificity in identifying drinking in pregnant women.[10] Most researchers and physicians rely on self-report of maternal alcohol use during pregnancy, with underreporting common because of stigmatization of drinking during pregnancy.[11] Alcohol use histories must be sensitively elicited to yield complete information. Studies indicate that obstetricians often obtain inaccurate consumption information. For example, in a prospective study that included high-risk women, almost twice as many admitted to drinking during a research assessment compared with indications from maternal medical records.[12]

Tools are available to assist physicians in accurately identifying women who consume alcohol during preg-

CME available online at www.jama.com

Author Affiliations: C. S. Mott Center for Human Growth and Development, Children's Research Center, and Departments of Obstetrics and Gynecology and Pediatrics, Wayne State University, Detroit, Mich (Drs Sokol and Delaney-Black); Department of Family Medicine, East Tennessee State University, Johnson City (Dr Nordstrom).
Corresponding Author and Reprints: Robert J. Sokol, MD, C. S. Mott Center for Human Growth and Development, 275 E Hancock, Detroit, MI 48201 (e-mail: rsokol@moose.med.wayne.edu).
Contempo Updates Section Editor: Sarah Pressman Lovinger, MD, and Catherine Meyer, MD, Fishbein Fellows.

nancy, especially at risk-drinking levels. One such tool is the T-ACE, an adaptation of a traditional alcohol screening test, the CAGE (a 4-item scale: Cut down, Annoyed, Guilty, Eye opener).[13] The T-ACE consists of 4 questions that may be asked as part of the history by physicians or office personnel (BOX).[13] It typically identifies 90% or more of potential risk-drinkers; false-positives can be determined with follow-up questions.[14]

Since the introduction of the T-ACE, several other alcohol screening tools for use with pregnant women have been developed or validated, including the TWEAK (Tolerance, Worry, Eye opener, Amnesia, Cut down), the Alcohol Use Disorders Identification Test (AUDIT), and the Short Michigan Alcoholism Screening Test (SMAST). Neither the AUDIT nor the SMAST has shown acceptable sensitivity (<20% in 1 recent validation study).[14] Although the TWEAK showed a reported 79% sensitivity in identifying at-risk drinking among pregnant women, the level of at-risk drinking identified is double the currently accepted definition of 1 drink per day.

Box. T-ACE Screening Tool for Pregnancy Risk-Drinking*

Tolerance

"How many drinks can you hold?"

A positive answer, scored a 2, is at least a 6-pack of beer, a bottle of wine, or 6 mixed drinks. This suggests tolerance of alcohol and very likely a history of at least moderate to heavy alcohol intake.

Annoyed

"Have people annoyed you by criticizing your drinking?"

Cut Down

"Have you felt you ought to cut down on your drinking?"

Eye Opener

"Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?"

*Adapted with permission from Sokol et al.[13] The first question is scored 0 or 2 points. The last 3 questions are scored 1 point if answered affirmatively. A total score of 2 or more is considered positive for risk-drinking.

Characteristics of Individuals With FAS or FASD

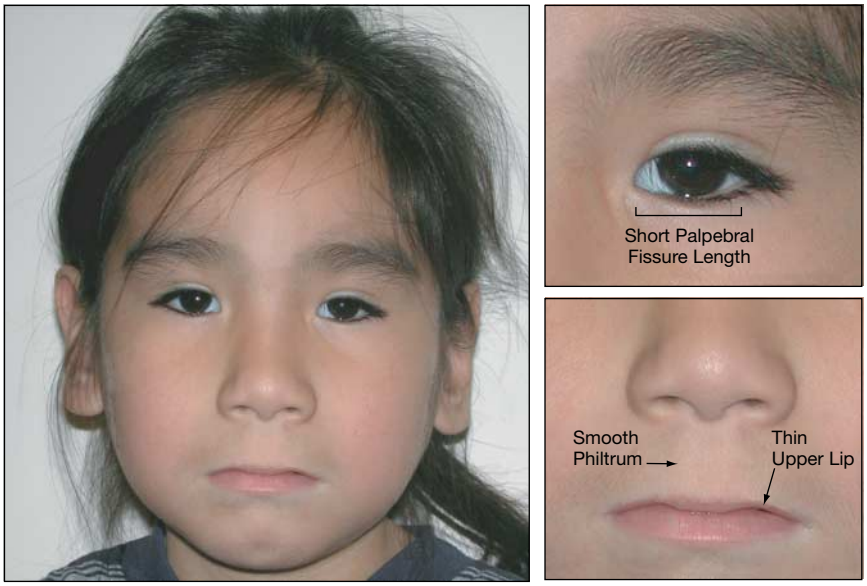
Individuals with FAS have characteristic facial dysmorphology (midfacial hypoplasia, long smooth philtrum, thin upper lip, small eyes that appear widely spaced, and inner epicanthal folds) (FIGURE); growth restriction, including relative microcephaly; and central nervous system and neurodevelopmental abnormalities, including ophthalmic involvement. As children, they typically struggle in school because of decreased cognitive functioning and social problems. Even with such outwardly visible characteristics, diagnosis is often delayed or missed entirely. In the prospective study previously described, infant chart review was also compared with prospective pregnancy research interviews.[12] Pediatricians failed to document exposure status in two thirds of cases in which women admitted to drinking during the research interview. One of 19 infants was identified as having possible effects of exposure, although in simultaneous research evaluations, 7 newborns had evidence of fetal alcohol exposure effects, including 2 with growth retardation, characteristic facial features, and microcephaly. Another study that included 6 children with FAS similarly revealed no pediatric diagnosis of FAS.[15] In a survey of family physicians, 49% indicated they had little confidence in their ability to diagnose FAS.[16]

Effects and Prevalence of Fetal Alcohol

Adverse behavioral effects in children exposed prenatally to risk levels as well as low and moderate levels of alcohol have been reported by many researchers. Neonatally, habituation to stimuli (lessening of response to repetitive stimuli) was most affected and at 8 months, significant effects were observed by using the Bayley Mental Developmental Index and Pyschomotor Developmental Index scales (global scales of infant behavioral functioning).[17] Furthermore, infants have longer reaction times when exposed prenatally to low to moderate levels of alcohol.[18] Decreased reaction time, inattention, and hyperactivity have been demonstrated in preschool children exposed to moderate levels of pregnancy drinking.[19] Learning problems,[20] attention and impulsivity problems,[21,22] memory deficits, distractability,[23] and psychiatric problems (most notably mood disorders)[24] have been identified in school-aged children exposed to moderate drinking levels. Children exposed to binge drinking were more likely to be classified as developmentally delayed in early childhood,[25] as having problems with distractibility, restlessness, and lack of persistence in preadolescence,[26] and with multiple neurobehavioral and other problems in adolescence.[27,28] Even prenatally exposed adults have been found to have attention problems,[29] executive functioning deficits leading to difficulty with problem solving and functioning in everyday life,[30] increased incidence of adult antisocial syndrome,[31] and higher rates of alcohol, drug, and nicotine dependence.[32]

These findings suggest that alcohol teratogenesis can affect academic and social functioning even with prenatal alcohol exposure at social drinking levels. Such exposure has been implicated as the most common cause of mental retardation and the leading preventable cause of birth defects in the United States, accounting for significant educational and public health expenditures.[2] The national incidence of FAS is probably in the 1 to 4.8 per 1000 range and the com-

Figure. Child With Facial Characteristics of Fetal Alcohol Syndrome



The 3 features used to diagnose the fetal alcohol syndrome (FAS) facial phenotype are short palpebral fissures, a smooth philtrum, and a thin upper lip, as exhibited by this child. Other minor facial anomalies may be also present in children with FAS. Reproduced with permission from Susan Astley, PhD, Director of the Washington State Fetal Alcohol Syndrome Diagnostic and Prevention Network.

bined incidence of FAS and FASD increases the prevalence of alcohol-related affected individuals to 9.1 per 1000 (nearly 1 in 100 births).[33] Knowledge of the incidence of FAS and FASD is limited and involves only estimates because no large-scale national incidence studies have been undertaken. We do know that substantially higher rates have been demonstrated among low socioeconomic and minority groups than among majority populations, with black children more than 5 times as likely and American Indian/Alaskan Native children 16 times more likely than white children to exhibit FAS.[34] Additionally, up to 50% of women of childbearing age consume alcohol[35] and 15% to 20% acknowledge continuing to drink during pregnancy.[36] Up to 1% of pregnant women drink at levels considered heavy,[2] with such consumption more common among women 30 years or older, unmarried, and with low incomes.[37]

Challenge of FASD Prevention

Universal efforts (broad public health measures) to prevent prenatal alcohol exposure have met with limited success. Education aimed at the general population has included public awareness campaigns and labeling alcoholic beverage containers with warning statements. For example, in 1981 the surgeon general issued a warning stating that there is no known safe level of alcohol consumption during pregnancy.[38] Had this universal public awareness approach been effective, rates of alcohol consumption among pregnant women and resultant rates of FAS and FASD should have decreased in the ensuing 2 decades. Unfortunately, studies suggest that the occurrence of FAS is actually increasing,[36] although this may be related to improved ascertainment.

In November 1989, alcoholic beverage container warning labels were introduced. A significant reduction in periconceptional alcohol intake occurred beginning in 1990, with an increase in knowledge of alcohol and pregnancy risk. However, the decrease in drinking was limited to women who were already light drinkers, with no significant change among those drinking at risk levels.[39] A report on 1989 to 1994 data showed no significant relation between exposure to warning labels and messages and drinking patterns during pregnancy.[40] Based on these findings, it appears that these universal approaches to reduce fetal alcohol exposure have not been successful, with the lack of success possibly related to differences between women who are risk drinkers and those who are not. Such differences could range from economic and educational status to genetic determinants of alcohol metabolic efficiency, all of which could produce differences in drinking behavior and in fetal vulnerability to adverse consequences of prenatal alcohol exposure.

What physicians do to decrease prenatal alcohol exposure depends on practice location and setting and the patient population being served. Focus should be on patients at increased risk for drinking during pregnancy and related adverse pregnancy outcomes. Examples of high-risk patients might include those in correctional facilities, drug and alcohol treatment facilities, family planning clinics, hospital emergency departments, migrant health centers, sexually transmitted disease clinics, and Women, Infants, and Children (WIC) clinics. In addition, some evidence exists that binge drinkers[25] as well as women 30 years or older who drink during pregnancy are at increased risk for delivering children with poor outcomes related to prenatal alcohol exposure.[41,42] The use of screening tools with these populations would identify at-risk women and allow the implementation of targeted prevention efforts.

Which prevention efforts are implemented for these patients will probably be determined by the training and expertise of the physician. Some obstetricians and an increasing number of primary care physicians have obtained training in cognitive behavior therapy or a version termed *motivational interviewing*, which helps empower the patient to make lifestyle changes.[43,44] In this empathic patient-centered counseling approach, the physician can illustrate the importance of abstinence or decreased alcohol intake and the avoidance of binge drinking and offer encourage-

ment and optimism about change. Research has suggested that pregnant women identified as heavy drinkers do respond to such treatment.[45,46] Follow-up is critical and studies have demonstrated that a series of such brief interventions (with booster sessions) are more effective than a single suggestion to stop drinking.[47,48]

For women of reproductive age who are receiving care in high-risk settings or who have other high-risk characteristics, routine use of a screening tool is warranted. For patients who score high, brief intervention to attempt to attain abstinence is warranted, along with appropriate follow-up. If the physician is not trained in these techniques, referral is appropriate. For women who are not at risk, selective prevention (general information about avoiding drinking during pregnancy) can be provided.

Conclusion

FAS and FASD continue to be significant medical and societal problems. Risk-drinking during pregnancy and the adverse consequences continue to be underidentified. To improve detection and outcomes, continued education of physicians concerning women who are at risk, available screening methods, and appropriate interventions and follow-up care are warranted. In addition, the development and testing of reliable biomarkers for identifying drinking in pregnant women would be desirable. A clinical focus on preconceptional and pregnant women is necessary to attain abstinence of alcohol during pregnancy and the reduction of FAS and FASD.

Acknowledgment: We thank the parents of the child whose face appears in this article for allowing us to use his photograph.

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