Fetal alcohol syndrome (FAS) is defined by specific diagnostic criteria as delineated by the National Center on Birth Defects and Developmental Disabilities (NCBDD), Centers for Disease Control and Prevention (CDC), and the National Task Force on Fetal Alcohol Syndrome and Fetal Alcohol Effect. It is one of the most common causes of developmental and intellectual disabilities in the US, occurring in 0.2–1.5/1000 births in the United States. Symptoms can range in severity but usually include a combination of physical, neurological, behavior, and learning problems. Children with the characteristic facial features, growth deficits, and central nervous system (CNS) abnormalities meet the criteria for FAS with or without documented prenatal alcohol exposure. For other disorders in the spectrum, as originally outlined by the Institute of Medicine (IOM), the full facial, growth, and CNS criteria for FAS may not be met but there must be confirmation of prenatal alcohol exposure. This is a narrow set of criteria that can miss many patients who have neurocognitive effects from alcohol exposure but do not have the classic triad essential for the diagnosis of FAS. In fact, research has shown that children who were exposed to alcohol in utero but do not meet the criteria for FAS have similar cognitive and behavioral characteristics.

Other disorders on the spectrum include Alcohol-Related Neurodevelopmental Disorder (ARND), Partial FAS (PFAS), and Alcohol-Related Birth Defects (ARBD). Using the revised Institute of Medicine Criteria set forth by Hoyme et al., ARND can be diagnosed in children with normal growth and structural development and who have characteristic cognitive or neurobehavioral abnormalities that are typical of prenatal alcohol exposure, including problems in executive functioning, communication, emotional lability, motor dysfunction, poor academic performance, deficits in social interactions, and unusual physiologic responses (including problems in sleep and hyperresponsiveness to sensory stimuli). Neurodevelopmental Disorder Associated with Prenatal Alcohol Exposure (ND-PAE) is the new terminology that has been proposed in the Diagnostic and Statistical Manual (DSM) V, and the criteria for the ND-PAE diagnosis is listed in the appendix of DSM-V. The proposed criteria includes that the patient was “exposed to alcohol at any time during gestation, including prior to pregnancy recognition and the exposure level was more than minimal” along with presence of neurocognitive impairment, impairment in self-regulation, and impairment in adaptive functioning. Minimal intake means “no more than 1–13 drinks per month and no more than 2 drinks per occasion.” Neurocognitive impairments in ND-PAE include global intellectual impairment, impairment in executive functioning, impairment in learning, impairment in memory, and impairment in visual–spatial reasoning. Impairment in self-regulation includes impairment in mood or behavioral regulation, attention deficit, and impairment in impulse control. Deficits in adaptive functioning include communication deficit, social impairment, impairment in daily living, and motor impairment. PFAS is diagnosed in the presence of facial
characteristics that meet the criteria for FAS and abnormalities in either in growth or in the CNS domain. ARBDs are diagnosed when there is confirmed exposure to alcohol in utero, normal growth, the typical facial characteristics, and specific structural abnormalities (either major malformations or a pattern of minor malformations). It is now known that relying on facial features for the identification of children with FASDs largely underidentifies the population of all alcohol-exposed pregnancies as the vast majority of individuals exposed to alcohol during pregnancy do not present with the FAS facial phenotype but rather with the CNS

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**TABLE 1.** The criteria for FAS diagnosis

A. Requires all three of the following findings:
   1. Documentation of all three facial abnormalities (smooth philtrum, thin vermillion, and small palpebral fissures).
   2. Documentation of growth deficits.
   3. Documentation of CNS abnormality.

B. Facial dysmorphia. Based on racial norms, individual exhibits all three characteristic facial features:
   1. Smooth philtrum (the University of Washington Lip–Philtrum Guide rank 4 or 5).
   2. Thin vermillion border (the University of Washington Lip–Philtrum Guide rank 4 or 5).
   3. Small palpebral fissures (at or below the 10th percentile).

C. Growth problems. Confirmed prenatal or postnatal height, or weight, or both, at or below the 10th percentile, documented at any one point in time (adjusted for age, sex, gestational age, and race or ethnicity).

D. Central nervous system abnormalities
   - Structural
     - Head circumference (OFC) at or below the 10th percentile adjusted for age and sex.
     - Clinically significant brain abnormalities observable through imaging.
   - Neurological
     - Neurological problems not due to a postnatal insult or fever or other soft neurological signs outside normal limits.
   - Functional
     - Performance substantially below that expected for an individual’s age, schooling, or circumstances, as evidenced by the following:
       1. Global cognitive or intellectual deficits representing multiple domains of deficit (or significant developmental delay in younger children) with performance below the 3rd percentile (2 standard deviations below the mean for standardized testing).
       2. Functional deficits below the 16th percentile (1 standard deviation below the mean for standardized testing) in at least three of the following domains:
          - Cognitive or developmental deficits or discrepancies.
          - Executive functioning deficits.
          - Motor functioning delays.
          - Problems with attention or hyperactivity.
          - Poor social skills.
          - Other (e.g., sensory problems, pragmatic language problems, or memory deficits).

E. Maternal alcohol exposure
   1. Confirmed prenatal alcohol exposure.
   2. Unknown prenatal alcohol exposure.
effects. Of all the conditions in the spectrum, ARND (more currently referenced as ND-PAE) is estimated to be 10 times more common than FAS.

The Facial and the Growth Criteria in FAS

The facial and the growth criteria are quite straightforward, but in order to evaluate the facial criteria, it is helpful to use the following: a clear plastic ruler with blunt edges and the University of Washington Lip–Philtrum guides (Fig 2). The Lip–Philtrum Guide (www.fasdpn.org) is a 5-point pictorial scale that measures the smoothness of the philtrum and the thinness of the upper lip. A rank of “1” on the scale depicts a deeply grooved philtrum and a thick upper lip; a rank of “5” depicts a smooth philtrum and thin upper lip that is characteristic of a child with FAS. There are two lip–philtrum guides. Guide 1 is used for Caucasians and all other races with lips similar to Caucasians. Guide 2 is used for African-American and all other races with lips as full as African-Americans. FAS facial features require a Rank 4 or Rank 5 lip and philtrum (Fig 2). Palpebral fissure length is measured using a clear plastic ruler from the inner to outer corners of the eye (the endocanthion to the exocanthion) and then the measurement is compared to a nomogram or plotted in an excel file using the following link: http://depts.washington.edu/fasdpn/pdfs/astley-pfil-zscore-calculator.xls; these would account for variations due to age. Further training on the diagnosis of facial criteria can be obtained by accessing the American Academy of Pediatrics FASD Pedialink at aap.org/fasd or the 4-Digit Diagnostic Code of the University of Washington. As defined in the 2004 NCBDD-CDC National Task Force guidelines, the growth criteria require the usual height and weight measures and is positive when there is confirmed prenatal or postnatal height, weight, or both at or below the 10th percentile documented at any point in time and adjusted for age, sex, gestational age, race, ethnicity, and even nutritional or genetic factors, when applicable.

The CNS Criteria for FAS

The CNS criteria for FAS can be met by documenting structural, neurological, or functional abnormality in FAS. The structural criteria are met either when there is a small head size (head size at or below the 10th percentile) or when there are structural abnormalities seen on imaging. Neurological abnormalities can be seen on exam and can consist of either focal findings (such as tremor) or unprovoked seizures. The CNS functional abnormalities are often best gauged by how the child thinks, learns, and behaves, as well as by reviewing information obtained from neuropsychological or developmental testing. Examples of CNS abnormalities are seen in Table 2.

In infancy, the CNS dysfunction may be characterized by poor suck and irritability. These infants may benefit from nutritional support and from decreasing environmental overstimulation. Toddlers with an FASD may appear to be very busy and distractible and may have problems with balance and coordination. They may also have difficulties in sleep and in managing sensory stimuli, and these items need to be noted by clinicians. Difficulties in sleep and in managing sensory stimuli may be manageable by guidance in the medical home but referrals to a sleep clinic and to an occupational therapy, respectively, may also be necessary. The toddler’s difficulties with comprehension and problem solving may result in prolonged tantrums. This problem becomes more evident in the preschool years when children are expected to have more self-regulation abilities. In fact, poor “self-soothing” appears to be one of the most common presenting symptoms of an alcohol-related neurodevelopmental disorder. Although early expressive language milestones may be normal, comprehension and understanding of concepts may lag behind and require language therapy. Furthermore, cause-and-effect reasoning is less efficient for children with FASDs, making it more difficult for them to learn from past experience.

Parenting can be confusing and challenging because these children may be able to repeat rules verbatim and yet may not be able to apply them to real-life situations. Behaviors will always have to be viewed through the lens of brain differences, and behavioral therapists need to realize this when planning interventions. School-age children with an FASD may continue to display the same struggles and, in addition, struggle with academic demands. Children with an FASD may struggle in all academic areas, but areas that appear to be most difficult include mathematics, writing, and language arts, not because of poor ability to decode the written word but due to difficulties in understanding abstract language. In addition, children with an FASD may exhibit slow processing of information. Poor attention and executive function may also limit academic progress. In addition, weak visual–spatial skills
Fig 2. Lip-Philtrum Guides 1 (A) and 2 (B) are used to rank upper lip thinness and philtrum smoothness. The philtrum is the vertical groove between the nose and upper lip. The guides reflect the full range of lip thickness and philtrum depth with Rank 3 representing the population mean. Ranks 4 and 5 reflect the thin lip and smooth philtrum that characterize the FAS facial phenotype. Guide 1 is used for Caucasians and all other races with lips like Caucasians. Guide 2 is used for African Americans and all other races with lips as full as African Americans. Copyright 2014, Susan Astley PhD, University of Washington. Copyright of the Picture(s) is not being released to the authors or publisher, only permission to incorporate it as described here.
and motor skills may adversely impact adaptive daily living skills. This is even more pronounced in the adolescent years when children are expected to do more and more for themselves. Individuals with a FASD may struggle from lack of social boundaries that make close supervision and instruction about boundaries that are mandatory for safety. In adolescence, social immaturity makes them an obvious target for bullies. Parents and teachers should be proactive about these issues and supervise social interactions of children and adolescents with an FASD. These could be addressed using social skills training. Finally, children and adolescents with an FASD should have a psycho-educational evaluation to inform implementation of appropriate educational interventions.14

Evaluating Maternal Alcohol Use

All clinicians should ask about maternal alcohol use, but sometimes it is challenging to obtain a positive history as in the case of foster or adoptive families, the information may be unavailable.

Pregnant women or biological mothers may feel stigmatized and therefore hesitant to report alcohol intake during pregnancy. There are available screening tools that are designed to identify risky drinking in pregnant women, one of which is the T-ACE.3,9–11 The T-ACE was discussed extensively in the article on Screening and Brief Interventions. The T-ACE considers any alcohol use during pregnancy as at-risk drinking. If all the diagnostic criteria (face, growth, and CNS) are present, FAS can be diagnosed even when maternal alcohol use is unknown. In order to document the exposure, a clinician could use clinical observation, self-report, reports of heavy alcohol use during pregnancy by a reliable informant, and medical records documenting positive blood alcohol levels or even treatment for alcohol abuse during pregnancy. In addition, any other social, legal, or medical problems related to drinking during the index pregnancy

<table>
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<tr>
<th>Table 2. CNS functional domains affected in FASD1</th>
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<td><strong>Functional domain</strong></td>
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<td>Cognitive or developmental deficits or discrepancies</td>
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<td>Executive functioning deficits</td>
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<td>Motor functioning delays</td>
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<td>Attention deficit or hyperactivity</td>
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<td>Poor social skills</td>
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<td>Other</td>
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*These examples are not exhaustive or mutually exclusive. All domains should be assessed using norm-referenced standardized measures and by appropriate professionals using reliable and validated instruments.
would be high risk for potential use. For ND-PAE, since the other physical criteria may not be present, in order to make the diagnosis, there should be history of more than minimal amounts of alcohol intake during pregnancy, which means “no more than 1–13 drinks per month and no more than 2 drinks per occasion.” Although ND-PAE cannot be diagnosed when alcohol intake does not meet the above criteria, there is no known safe amount or timing of alcohol use during pregnancy.

**Other Physical Findings in FAS/FASDs**

As noted above, three facial features are considered to be central to the diagnosis of FAS: short palpebral fissures, a thin vermillion border or upper lip, and a smooth or flattened philtrum. A number of other physical anomalies are associated with but not necessarily unique to prenatal alcohol exposure. These include epicanthal folds, ptosis, strabismus, “railroad track” ears, small upturned nose, flattened nasal bridge, maxillary hypoplasia, dental malocclusions, cleft palate, narrow- or high-arched palates, “hockey stick” or other abnormal palmar creases, camptodactyly and clinodactyly, nail hypoplasia, joint contractures, and cardiac defects.

**Differential Diagnosis of FAS/FASDs**

Some of the craniofacial features that make up the facial dysmorphia of FAS may be confused with other genetic or teratogenic syndromes. The craniofacial features of FAS that may be confused with other syndromes are smooth philtrum (the University of Washington Lip–Philtrum rank 4 or 5), thin vermillion border (ranks 4 or 5), and short palpebral fissures (at or below the 10th percentile for racial norm). Smooth philtrum is seen in Opitz syndrome, Cornelia de Lange syndrome, Toluene embryopathy, Floating–Harbor syndrome, and Geleophysic dysplasia. Thin vermillion border is seen in Miller–Dieker syndrome, Cornelia de Lange syndrome, Toluene embryopathy, Geleophysic dysplasia, and fetal valproic acid syndrome. Short palpebral fissures are features of Toluene embryopathy, Williams syndrome, Trisomy 18 syndrome, maternal phenylketonuria (PKU) fetal effects, Campomelic dysplasia,
22Q11.2 deletion syndrome, Opitz syndrome, FG syndrome, Dubowitz syndrome, chromosome 10q duplication syndrome, chromosome 15q duplication syndrome, and Oculodentodigital syndrome. Some of the neurobehavioral features of FAS may be seen in syndromes such as Fragile X syndrome, 22Q11 deletion syndrome, Opitz syndrome, Turner syndrome, and even in traumatic brain disorder, but the triad of problems in neurocognition, poor adaptive skills, and poor self-regulation have been recognized by many experts as common features of the FASDs. Further research needs to examine the level of specificity of this triad of findings, and this is one of the conditions under study in the Diagnosis and Statistical Manual of Mental Disorders-5 (DSM-5). Prenatal and/or postnatal growth deficiency is seen in several chromosome and single gene disorder syndromes. Several of these syndromes have other features that help the diagnostician to discriminate them from FAS and the FASDs. Tables 3 and 4 summarize some of the genetic syndromes with overlapping craniofacial or neurobehavioral features with FAS.

### Summary

FASDs are the most common preventable cause of developmental and intellectual disabilities in the United States and yet can easily be overlooked in pediatric and adolescent practices. Early diagnosis, presence of developmental and educational services, and a nurturing home environment have been associated with decreased occurrence of secondary disabilities such as substance use and criminal involvement. Therefore, it is important for providers to know how to go about the identification, diagnostic, and evaluation process. Pediatric care clinicians should be knowledgeable about the diagnostic criteria for fetal alcohol syndrome and know common differentiating conditions. Furthermore, they should be able to recognize other disorders on the spectrum, and in doing so, they should facilitate appropriate referral, initial management, and coordination of care.

### References

2. Astley S. Palpebral fissure picture (has consent—will be released to Elsevier).


