

ATTEMPTS AT MORE SPECIFIC AND PRACTICAL DIAGNOSTIC CRITERIA FOR FETAL ALCOHOL SPECTRUM DISORDER

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A CRITICAL REVIEW of “A practical clinical approach to diagnosis of fetal alcohol spectrum disorders: Clarification of the 1996 Institute of Medicine criteria.” Hoyme H, May P, Kalberg W, Kodituwakku P, Gossage JP, Trujillo PM, Buckley DG, Miller JH, Aragon A, Khasle N, Viljoen DL, Jones K, Robinson KL. *Pediatrics*. 2005;115(1):39-47.

The adverse effects of alcohol on the developing human represent a spectrum of structural anomalies, behavioral and neurocognitive disabilities, most accurately termed Fetal Alcohol Spectrum Disorder (FASD).¹ Two sets of diagnostic criteria are now used most widely for evaluation of children with potential diagnoses in the FASD: the 1996 Institute of Medicine (IOM) criteria² and the Washington University criteria.³ Although both approaches have improved the clinical delineation of FASD, both have significant drawbacks in their application in pediatric practice.

The IOM criteria are vague, with no specific parameters set forth for diagnosis in each category. First, neither the degree of growth deficiency nor the exact facial dysmorphic features required for each category have been defined. In addition, the specific behavioral/cognitive phenotype is not characterized. Second, assessment of the family and genetic history of each affected child is not addressed adequately. Finally, alcohol-related birth defects (ARBD) and alcohol-related neurodevelopmental disorder (ARND) are not practically defined in a clinical sense. Because of these concerns, Astley and Clarren sought to develop a more

objective set of diagnostic criteria for FASD, which was published in 2000.

Their criteria retain the four commonly accepted key diagnostic features of FAS, i.e., growth deficiency, characteristic FAS facial phenotype, central nervous system damage/dysfunction, and alcohol exposure *in utero*. But the Washington criteria place more emphasis on the encephalopathy and neurobehavioral disorder present among affected children that are not unique to the prenatal effect of alcohol.⁴ In addition, the family and genetic background of the child are not adequately integrated into the criteria and there is the potential for overdiagnosis of alcohol-related disabilities.

The multi-center study that we review here was an attempt to clarify the 1996 IOM criteria for the diagnosis of FASD, and to facilitate their practical application in clinical pediatric practice. IOM diagnostic criteria for FASD were evaluated by the authors during a period of 5 years, among high-risk populations in the United States and South Africa.^{5,6} The American subjects were from 6 Native American communities and one urban population each in Montana, North Dakota, and South Dakota. The South African subjects were enrolled from one community in the wine-producing region of the Western Cape.

The American children were referred because of developmental and/or behavioral problems and possible prenatal alcohol exposure, whereas the South African children were part of a school-based screening program involving all children in first grade in the targeted community.

All subjects underwent comprehensive multidisciplinary evaluations in three areas:

1. Growth and structural development (assessed independently by a minimum of 2 dysmorphologists, adhering to a protocol),
2. neuropsychological, intellectual and social development, and
3. maternal risk factors (assessed with a comprehensive maternal interview).

Matched control children were examined in a blinded manner.

After the data were gathered for all three domains, each child was assigned to a FASD diagnostic category or another diagnosis, in a case conference.

The facial morphologic features of the subjects, i.e., palpebral fissure length and the morphologic features of the philtral ridges and upper lip, were assessed. Palpebral fissure measurements were obtained with a rigid ruler. Upper lip and philtrum were assessed and scored with the lip/philtrum guide described by Astley and Clarren. The subjects underwent a battery of developmental and neuropsychologic tests, including broad measures of IQ and behavioral and social development and narrow-band tests of performance on complex tasks (typified by assessment of higher executive control functioning). Examiners included psychologists, a neuropsychologist, a developmental pediatrician, and an educational diagnostician. Structured interviews of the biological mothers including 300 items on the subjects were conducted to determine the amount and frequency of alcohol intake during pregnancy. Of the 1500 children evaluated, 164 children with a potential FASD diagnosis were identified, i.e., 72 Native American children and 92 South African children. Based on the results, the authors suggested some clarifications to the 1996 IOM diagnostic guidelines.

In the proposed clarifications of the IOM criteria, children with FAS (with or without confirmed maternal alcohol exposure) must have abnormalities in all domains, i.e., facial dysmorphic features, growth, and brain

growth or structure. In the partial FAS category (with or without confirmed maternal alcohol exposure), children must display typical facial dysmorphic features and abnormalities in one of the other domains (growth or central nervous system structure or function).

The term ARBD is meant to apply to affected children in the FASD continuum who have typical facies, normal growth and development, and specific structural anomalies (either major malformations or a pattern of minor malformations). ARND is meant to apply to children with normal growth and structural development who display a characteristic pattern of behavioral or cognitive abnormalities typical of prenatal alcohol exposure. In this latter category, the authors felt it is imperative that the neurobehavioral abnormalities not be typical of other individuals in the family who were not exposed prenatally to alcohol. In addition, the abnormalities should not be explained by postnatal environmental influences alone. The behavioral profile of children with FASD includes: marked impairment in the performance of complex tasks (complex problem solving, planning, judgment, abstraction, metacognition, and arithmetic tasks); higher-level receptive and expressive language deficits; and disordered behavior (difficulties in personal manner, emotional lability, motor dysfunction, poor academic performance, and deficient social interaction).^{7,8}

The Hoyme study is an attempt to specify diagnostic criteria for FASD and to distinguish it from other relatively similar conditions. For the first time the authors assert that in all categories of FASD, except ARND, it is critical to have evidence of a characteristic pattern of facial anomalies (at least two out of three). The authors in their criteria clearly defined the degree of growth deficiency and specified the facial anomalies and measurements that they considered to be

abnormal. ARBD and ARND were specifically defined. For the first time, the authors of this study attempted to adhere to criteria of FASD based not only on prenatal alcohol exposure but also based on elimination of known genetic and malformation syndromes.

This overall good study has some serious limitations. The normative values used to define the degree of growth deficiency and facial morphological features were largely based on a white population, not on a variety of racial backgrounds. The absence of such specific racial/ ethnic group- based data is a serious obstacle to the validity of these criteria. In addition, the authors never mention how the control group was gathered and matching criteria were not described. Many of biological mothers for American children were not available, so retrospective structural interview of the mothers to determine the amount and frequency of alcohol intake during pregnancy were not complete. Those interviews that were available had probably some degree of recall bias. It is mentioned but not explained how the authors assessed children for postnatal environmental influences.

Finally, the most concerning issue is the authors' suggestion that a diagnosis of ARND can be derived based on some facial dysmorphology and growth delay, without CNS impairment and confirmation of alcohol exposure. This approach may misdiagnose a large number of children with failure to thrive and metabolic and genetic disorders, and contradicts current knowledge that CNS impairment is the leading sign of fetal alcohol toxicity. As the authors conceded, ARND remains the weakest category in terms of diagnostic criteria and should be studied further.

Critically, while FASD is a condition that affects mostly brain development, the authors are geneticists. It would have been useful to have neurobehavioral scientists deal with the

most challenging elements of diagnosis, namely the "brain domain."

In conclusion, this study is important because it has not only brought much needed attention to the current insufficiency in diagnostic criteria for FASD, but also proposed new, more specific and practical diagnostic criteria. Despite the fact that the study has some serious limitations, it is an important attempt to distinguish FASD from other genetic and malformation syndromes. The lack of serious discussion of the "brain domain" is a major weakness.

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