

Recognition of Facial Features of Fetal Alcohol Syndrome in the Newborn

JOAN MARILYN STOLER* AND LEWIS BALL HOLMES

The diagnosis of an infant, especially a newborn, with fetal alcohol spectrum disorder is difficult due to the fact that not all of the features are apparent at that time. Many cases are also missed due to inadequate knowledge of the mother's drinking pattern and because of the examining physician's lack of experience with the disorder. While conducting a study of the use of maternal blood markers to determine alcohol use in pregnancy, we have evaluated systematically the effects of alcohol on the newborn infant. We have developed a facial scoring system consisting of six of the features commonly seen in children with fetal alcohol syndrome (FAS) and present preliminary data about its use. By using a cutoff of four or more of these six features, there is a significant correlation with the presence of these features and the mother's self-reported alcohol use. In addition, there has been no significant difference in the frequency of positive scores between newborns of Caucasian or Black ancestry. We propose that this system may be useful in the assessment of newborn infants at high risk because of alcohol exposure during pregnancy. © 2004 Wiley-Liss, Inc.

KEY WORDS: fetal alcohol spectrum disorder; facial features; diagnostic criteria; newborn and early infancy

IMPORTANCE OF EARLY DIAGNOSIS OF FETAL ALCOHOL SPECTRUM DISORDER

It has become apparent that the early diagnosis of fetal alcohol syndrome (FAS) or the lesser effects, referred to by different names (fetal alcohol effects (FAE), partial FAS, alcohol-related neurodevelopmental disorder, fetal alco-

hol spectrum disorder), plays a role in how well these children do. Streissguth et al. [1996] demonstrated that the protective factors associated with better outcome are early diagnosis, a stable living environment, and eligibility for special services. This holds true for both children with full FAS and those with the lesser effects. Surprisingly, the individuals with more secondary disabilities, such as school and job failure and legal difficulties, were those who had higher IQs and had the lesser effects. One of the reasons proposed for this was the fact that these children were not diagnosed early and did not receive the appropriate services in infancy.

CRITERIA FOR THE DIAGNOSIS

Inadequate criteria for diagnosis were thought to be one of the reasons for the failure of alcohol-exposed children to be recognized and diagnosed early. The Institute of Medicine proposed a series of criteria for diagnosis [Stratton et al., 1996], whose aim was to clarify this situation. For FAS, it was divided first into those with confirmed maternal alcohol exposure and those without confirmed maternal exposure, taking

into consideration the fact that in many cases the maternal history is not available when the diagnosis is being considered. For FAS [Stratton et al., 1996] to be diagnosed the following was required:

1. Confirmed maternal exposure
2. The presence of "a characteristic pattern of facial anomalies," including short palpebral fissures and abnormalities in the premaxillary zone (such as thin upper lip, flattened philtrum, and flat midface)
3. Growth retardation (low birth weight for gestational age, decreasing weight over time unrelated to nutrition, and disproportionately low weight to height)
4. Central nervous system (CNS) neurodevelopmental abnormalities, consisting of at least one of:
 - a. Decreased head size at birth
 - b. Structural brain anomalies (such as microcephaly, partial or complete agenesis of the corpus callosum, and cerebellar hypoplasia)
 - c. Neurological hard or soft signs (appropriate for age), including impaired fine motor skills, neurosensory hearing loss, poor tandem gait, and poor eye-hand coordination.

Dr. Stoler is a medical geneticist at Massachusetts General Hospital and Assistant Professor of Pediatrics at Harvard Medical School. Her research interests have been focused on fetal alcohol syndrome and methods of its prevention.

Dr. Holmes is chief of the Genetics and Teratology Unit at the Massachusetts General Hospital and Professor of Pediatrics at Harvard Medical School. He has worked for many years in clinical genetics and his research has focused on studying the teratogenic effects of various medications and exposures.

Grant sponsor: ATPM/CDC/ATSDR Cooperative Agreement; Grant sponsor: Genesis Fund, Boston.

*Correspondence to: Joan M. Stoler, Genetics and Teratology Unit, Massachusetts General Hospital, 55 Fruit St. Warren 801, Boston, MA 02114.

E-mail: jstoler@partners.org

DOI 10.1002/ajmg.c.30012

Instead of FAE, the term partial FAS was recommended. The criteria for this diagnosis included, in addition to confirmed maternal alcohol exposure and evidence of some of the characteristic facial features:

1. Growth retardation
2. Neurodevelopmental anomalies (as above)
3. Evidence of a complex pattern of behavioral or cognitive abnormalities "that are inconsistent with developmental level and cannot be explained by familial background or environment alone, such as learning difficulties, deficits in school performance, poor impulse control, problems in social perception, deficits in higher level receptive and expressive language, poor capacity for abstraction or metacognition; specific deficits in mathematical skills or problems in memory, attention or judgment."

Two other categories were also created, neither of which fit clearly into either FAS or partial FAS: 1) alcohol-related birth defects and 2) alcohol-related neurodevelopmental disorder for clinical conditions. The criteria for alcohol-related birth defects included the history of exposure plus a series of congenital anomalies known to be associated with prenatal alcohol exposure. The criteria for alcohol-related neurodevelopmental disorder included the presence of the neurodevelopmental anomalies listed above and/or the behavioral and cognitive problems listed above. The term *fetal alcohol spectrum disorder* is now used to encompass all of the manifestations of damage from fetal alcohol exposure.

FACIAL FEATURES

The classical facial features of FAS are short palpebral fissures, epicanthal folds, midface hypoplasia, depressed wide nasal bridge, anteverted nares, long hypoplastic philtrum, and a thin upper vermilion border (Figs. 1 and 2). There is concern that some of these features, such as epicanthal folds and depressed wide nasal

The classical facial features of FAS are short palpebral fissures, epicanthal folds, midface hypoplasia, depressed wide nasal bridge, anteverted nares, long hypoplastic philtrum, and a thin upper vermilion border.

bridge, occur more frequently in certain ethnic groups, perhaps resulting in overdiagnosis in these ethnic groups. Astley and Clarren [1995] analyzed these features and showed that the most discriminant features were short palpebral fissures, smooth philtrum, and thin upper vermilion border. They showed that these features best differentiated children with and without FAS with 100% sensitivity and 87% specificity. In addition, these three features were unaffected by race, gender, or age.

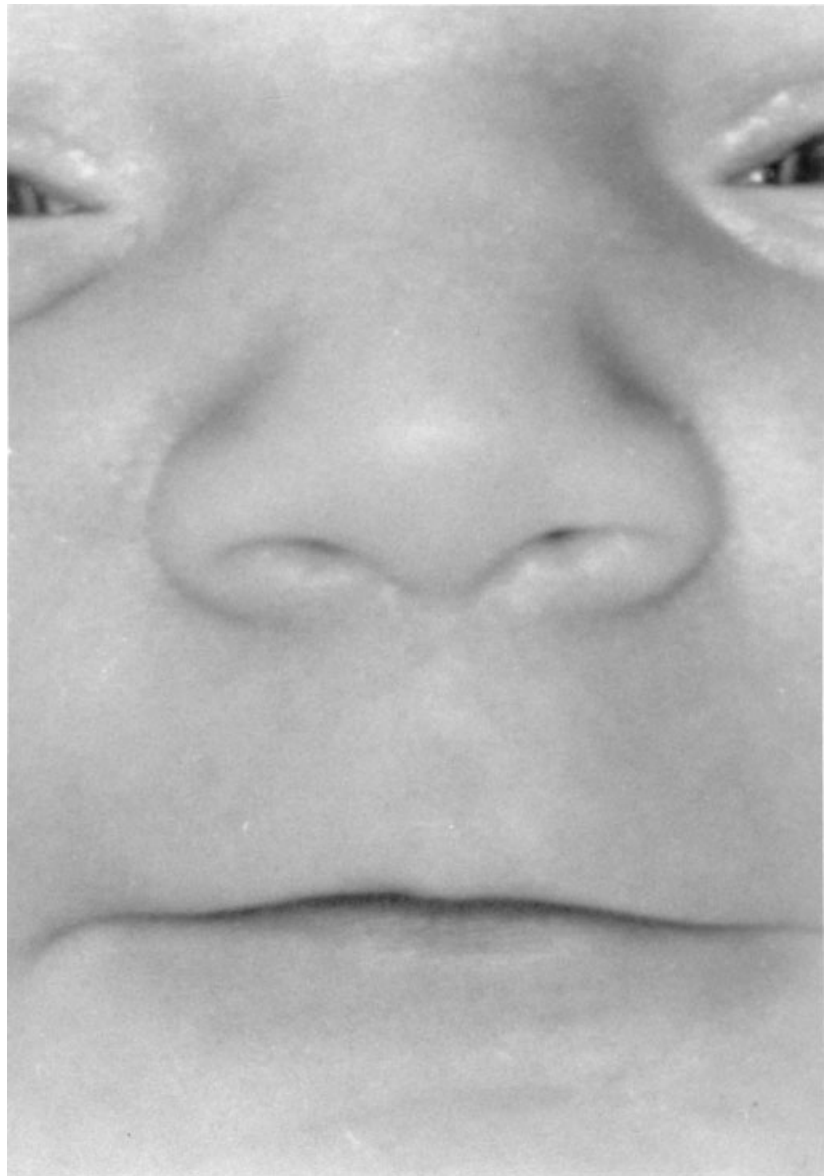


Figure 1. Infant with long upper lip, flat philtrum, thin vermilion, broad depressed nasal bridge, and anteverted nares. Reproduced with permission by Mosby, Stoler et al., 1999.



Figure 2. Infant with depressed nasal bridge, long upper lip, flat philtrum, and thin vermilion. Reproduced with permission by Mosby, Stoler et al., 1999.

UNDERDIAGNOSIS IN THE NEWBORN PERIOD

These criteria are appropriate for the evaluation of an older child when it would be possible to assess the neurodevelopmental, cognitive, and behavioral patterns. However, it can be difficult to apply these criteria exactly in a newborn or young infant. Accordingly, it is presumed that many cases of both FAS and partial FAS are missed in the newborn period. One problem with the identification of at-risk babies is not

knowing which infants have been exposed, as many women underreport their use of alcohol in pregnancy [Ernhart et al., 1988]. Ernhart et al. [1995] also showed the difference between detection in a research vs. a clinical setting. For example, one baby was diagnosed during their follow-up study with FAS with mental and growth retardation. However, this child would not have been identified clinically due to the mother's initial reports of no alcohol use in pregnancy. Another reason is that clinicians often do not recognize that

their nonminority patients are at risk for having alcohol-damaged infants because they believe this exposure is more of a problem among minorities [Nanson et al., 1995] and are reluctant to label their patients as users.

Clinicians often do not recognize that their nonminority patients are at risk for having alcohol-damaged infants because they believe this exposure is more of a problem among minorities and are reluctant to label their patients as users.

In addition, many cases have been missed, even when the exposure is known. For example, Little et al. [1990] studied 40 infants born to 38 known alcohol abusers. None of these infants were diagnosed by the examining pediatricians as having FAS or FAE, when in actuality 6 of the 40 infants had features of FAS. Similarly, we studied the medical records of babies and their mothers in a large prospective study of biomarkers of alcohol use in pregnancy [Stoler et al., 1998]. We reviewed the medical records of 19 newborn infants with documented maternal history of alcohol use [Stoler and Holmes, 1999]. None of these infants were identified as having alcohol-related features by the examining pediatricians, despite the notation of the mother's drinking in the chart. Each of these 19 infants was assessed, using specific criteria for evidence of prenatal alcohol damage (the presence of the cardinal facial features of FAS and growth retardation, described in detail below), by a dysmorphologist blinded to the exposure. Two of these infants were judged as showing possible signs of FAS.

Intrauterine growth retardation is one of the components of the diagnostic criteria. Certainly there are many causes of intrauterine growth retardation, with

alcohol exposure being only one of many. However, in the face of exposure, such growth retardation is significant [Khoury et al., 1996]. We have also found this to be the case, as discussed above [Stoler and Holmes, 1999]. Similarly, microcephaly is a significant component of the diagnostic criteria. When assessing a child with microcephaly, the possibility of alcohol exposure should be kept in mind as one of many different etiologies.

PHYSICIANS' KNOWLEDGE OF FAS

One reason for underdiagnosis may be due to pediatricians being unfamiliar with the characteristic features. Morse and Weiner [1990] demonstrated that primary care physicians typically underdiagnose FAS. A survey of pediatricians in Massachusetts by this group [Morse et al., 1992] showed that pediatricians in general are unprepared to deal with FAS and its implications. More pediatricians

Morse and Weiner [1990] demonstrated that primary care physicians typically underdiagnose FAS. A survey of pediatricians in Massachusetts by this group [Morse et al., 1992] showed that pediatricians in general are unprepared to deal with FAS and its implications.

suspected the diagnosis than actually diagnosed it. Three-quarters of the pediatricians stated that they would find professional education about FAS to be beneficial.

There is also inadequate knowledge of the whole spectrum of effects beyond FAS. Therefore, milder cases may be missed more. Even though these cases are milder in that the affected individuals may have fewer signs and do not fit all of the diagnostic criteria, they may have

more impairment in their functioning. Streissguth et al. [1996] showed that individuals with FAE were more likely to have more secondary disabilities, such as school and job failure. Nanson et al. [1995] found that more physicians are aware of FAS than of the entire spectrum. Pediatricians were more aware of the spectrum of FAS than family practitioners or general practitioners. Clearly, more education about the effects of prenatal alcohol exposure should be included in the medical training of not only pediatricians, but also family practitioners.

Physicians in general have inadequate knowledge of the dose/effect ratio for alcohol effects. Abel and Kruger [1998] surveyed physicians and found that 41% reported the threshold for FAS as being one to three drinks per day, clearly an underestimate of the critical amount. While lower IQ and reduction in birth weight and head circumference can be seen at lower amounts of exposure (Table I), FAS is associated with an exposure of approximately an average

While lower IQ and reduction in birth weight and head circumference can be seen at lower amounts of exposure FAS is associated with an exposure of approximately an average of 4 ounces of absolute alcohol per day (roughly eight drinks per day).

of 4 ounces of absolute alcohol per day (roughly eight drinks per day) [Clarren et al., 1987].

Pediatricians may also be more focused on other exposures, such as cocaine, rather than alcohol. In our study on the underrecognition of FAE in newborns, the pediatrician noted the presence or absence of a history of exposure to cocaine in 98% of the newborns' medical records, compared to only 48% for alcohol exposure [Stoler and Holmes, 1999].

Another problem reflecting lack of familiarity with the diagnostic criteria is overdiagnosis in some cases. There are other conditions, which can share some of the facial features, such as mid-face hypoplasia (Table II). We reported several cases of misdiagnosis [Stoler, 1999] in which children were diagnosed as having FAS but had other diagnoses, such as velocardiofacial syndrome. Not being aware of their other conditions did impact their medical care. Of course, some of these children were also alcohol exposed, which may have contributed to the severity of their problems.

More sensitization of these effects among examining pediatricians and uniform criteria are needed to standardize and facilitate the diagnosis of these children. Several groups have tried to deal with this problem. Astley and Clarren [1995] have developed an approach using a coding system, but this method has been difficult to implement. The Institute of Medicine developed the series of criteria outlined above, and the Centers for Disease Control currently has a task force devoted to this. While criteria have been proposed, it is

TABLE I. Dose and Effects of Fetal Alcohol Exposure

Feature	Amount
FAS	≥4 ounces of absolute alcohol ^a /day
Decreased birth weight	2–3 ounces of absolute alcohol/day
Decreased I.Q. (5–7 points)	1.5 ounces of absolute alcohol/day
Spelling and reading difficulties	≥0.5 ounces of absolute alcohol/day
Functional deficits	5 drinks/occasion 1×/wk
Hyperactivity, inattention	0.45 ounces of absolute alcohol/day

^aOne standard drink = 0.48 ounces of absolute alcohol.

[Clarren et al., 1987; Jacobson et al., 1994; Larroque et al., 1995; Streissguth et al., 1996, 1998].

TABLE II. Conditions Sharing Some of the Same Features as FAS

Fetal anticonvulsant embryopathy
Fetal toluene exposure
Infant of mother with phenylketonuria
Velocardiofacial syndrome
Noonan syndrome
Pyruvate dehydrogenase deficiency

very difficult for these criteria to be incorporated into a reliable diagnostic schema that could be used across many different centers. In this paper we present our experience in using a facial score with measurement of facial features in the newborn period in the hopes of increasing reliability of assessment of these features.

EXPERIENCE WITH ASSESSMENT OF NEWBORN INFANTS

Previous and Ongoing Studies

We have conducted a prospective study of the effectiveness of four maternal blood markers (whole blood-associated acetaldehyde, carbohydrate-deficient transferrin, gamma-glutamyl transferin, and mean red blood cell volume) of alcohol use for identifying pregnant women at risk for alcohol-damaged babies [Stoler et al., 1998]. We compared the findings for blood markers to those from self-reporting measures: 1) the TWEAK, an alcoholism screening questionnaire, validated in several groups of pregnant women [Bradley et al., 1998]; and 2) an in-depth interview, using the timeline follow-back method of determining alcohol intake [Sobell and Sobell, 1992]. We also compared the marker results and the women's self-report to the effects on the infants. Therefore, we needed to have an accurate assessment of the alcohol effects in the newborn. The examinations were done by either of two study dysmorphologists who were unaware of the baby's exposure status.

An infant was judged to be affected if one or more of the following features were present: 1) evidence of growth retardation, with head circumference and/or low birth weight and/or birth length greater than or equal to two standard deviations below the mean, adjusted for gender and gestational age; and 2) a positive facial score. An infant with both growth retardation and a positive facial score was considered to have FAS; the infant with one of these findings was considered to have possible partial FAS or FAE. There are many causes of growth retardation and therefore we used the designation "possible" partial FAS or FAE when only one of the criteria was met.

There are significant difficulties in making the diagnosis in the newborn period, as the potential neurological, cognitive, and behavioral effects will not be apparent. Therefore, we eliminated this component of the diagnostic criteria. In addition, some of the facial features are hard to analyze accurately, specifically midface hypoplasia and palpebral fissure size. We rarely succeed in measuring with calipers the length of the palpebral fissures due to the swelling of the eyes that is common in newborn infants and also the fact that most newborn infants do not open their eyes long enough to make measurements possible. We did not use the palpebral fissure length for scoring purposes due to the fact that we were not able to assess it in each infant. If the baby had his/her eyes open voluntarily, we did note whether the palpebral fissures appeared short and measured them.

In tabulating the facial score, one point is given for the presence of each of these six features: depressed nasal bridge, wide nasal bridge, anteverted nares, long philtrum, hypoplastic philtrum, and thin upper vermilion. A baby is considered to have a positive facial score if he/she has four or more of these six features present. The requirement for four or more features was chosen because some of these features, such as broad nasal bridge, are common in some ethnic groups without alcohol exposure. The scores were given after the examination was completed. The research

assistant, who was unaware of the physician's assessment, took photographs of the face. These photographs were used to facilitate retrospective reviews of the face. In addition to this subjective assessment, measurements were made of head circumference, birth length, inner-canthal distance, and length of nose and philtrum. There was a good correlation between the measurements of the inner-canthal distance and the length of the philtrum with the clinical assessment of the width of the nasal bridge and length of the philtrum [Stoler et al., 1998]. The centile of each measurement is based on the gestational age of each infant [Hall et al., 1989].

The mothers were recruited from several urban hospitals, from general obstetric clinics, and a high-risk substance abuse clinic [Stoler et al., 1998]. The hospitals were chosen for the varied populations they serve. Currently, these maternal blood markers of alcohol use are being used to identify at-risk pregnancies and as a marker of change in drinking behavior after motivational intervention. We are using the same manner of assessing the infants, including the facial scoring system, in the ongoing intervention study.

Results of the Facial Scoring System

There were 293 babies on whom facial scores were established and whose mothers were interviewed. Fifty-two percent of these babies were Caucasian, 22% were Black, 3% were Hispanic, 2% were Asian, and the rest were of mixed ancestry.

The facial score rating was analyzed in several different ways:

1. Facial score and self-report. There was a significant difference in the percentage of babies with positive facial scores whose mothers reported significant (daily or weekly) alcohol use during the pregnancy compared to those who did not (Table III). However, the number of mothers ($n = 17$) who reported heavy alcohol use during pregnancy was small.

TABLE III. Facial Score and Self-Report

Alcohol measure	Facial score ^a		Accuracy	Sensitivity	Specificity
	Positive n (%)	Negative n (%)			
Alcohol use ^b					
Yes	4 (14.8)	13 (4.9)	87.7	23.5	91.7
No	23 (85.2)	253 (95.1)			
	$\chi^2: P < 0.035$				
TWEAK					
Positive ^c	5 (33.3)	16 (13.2)	81.4	23.8	91.6
Negative	10 (66.7)	105 (36.7)			
	$\chi^2: P < 0.035$				

^aDefined as having four or more of the following six features: epicanthal folds, depressed nasal bridge, wide nasal bridge, long philtrum, hypoplastic philtrum, and/or thin upper vermilion.

^bDefined as daily or weekly alcohol use throughout the pregnancy.

^cPositive TWEAK defined as three or more out of a total score of 7.

2. Facial score and TWEAK. Of the babies with positive facial scores, 33% of their mothers had positive TWEAK scores compared to 13% of those with negative facial scores whose mothers had positive TWEAK scores (Table III). While the sensitivity of the score was low, the specificity was quite high.
3. There were three babies who were small for gestational age and who had positive facial scores. All of the mothers of these infants had a positive TWEAK score or reported some alcohol use during pregnancy. There were four babies with small head circumferences and positive facial scores, one of whose mother had a positive TWEAK score.
4. Facial score by ethnicity. Nine percent of the Caucasian babies whose mothers reported no alcohol use during the pregnancy had positive facial scores compared to 12% of the Black babies, a difference that is not statistically significant. Seventeen percent of the babies of the Asian and 11% of the Hispanic mothers who reported no alcohol use had positive facial scores; however, these sample sizes were quite small.

CONCLUSIONS

Development of an easy-to-use diagnostic tool for assessment of FAS in the

newborn period would be valuable for both clinicians and researchers. For clinicians, it could be used in their evaluations of babies who are at high risk because of a known history of maternal alcohol use. Then with early identification, an alcohol-exposed newborn infant with physical evidence of effects, such as a positive facial score, could receive more intensive follow-up and have appropriate services. This would reduce the delay in these children being diagnosed. For researchers, it would help to ensure consistency in the assessment of newborn infants who are part of various studies, such as those aimed toward prevention.

We are encouraged that this facial scoring system may prove to be a helpful adjunct in the assessment of alcohol-exposed newborns. The facial scoring system correlates with the infant exposure status as measured by self-report from an in-depth interview and an alcoholism screening questionnaire. When using a cutoff of the presence of four or more of the designated features, there

The sensitivity of the facial score was low, but the specificity and overall accuracy was relatively high.

was no significant difference between the different ethnic groups, although the numbers of Hispanic and Asian patients were small. The sensitivity of the facial score was low, but the specificity and overall accuracy was relatively high (Table III). There are many reasons why the sensitivity would be low. First of all, not all alcohol-exposed infants are affected or affected to the same degree. In addition, this screen will not detect children who do not have the facial features but who will manifest the cognitive or behavioral aspects of the fetal alcohol spectrum disorder. Our time frame was limited to the immediate newborn period and we could not correlate the newborn findings with the child's physical features later on. Clearly, this has to be done to confirm the predictive value of this method.

Such a scoring system has potential advantages in that it would be quick and easy to use once a physician is familiar with the features. However, there are significant limitations. First of all, physicians would need to be trained in the assessment of these features in a consistent manner. A careful definition of the physical features is required. Physicians would need to have some method of verification. While there was a significant correlation with the self-report and the score, we do not know yet whether a positive facial score indicates the presence of the alcohol-related features in later childhood. Clearly more work needs to be done to validate this system.

Of course, this checklist does not address the issue of better identification of babies who are at high risk for alcohol effects. Efforts continue to develop better methods of detecting these high-risk pregnant women. Further work is needed to validate the predictive value of maternal blood markers during pregnancy and other markers, such as the analysis of fatty acid ethyl esters in meconium [Bearer et al., 1992].

ACKNOWLEDGMENTS

This work would not be possible without the cooperation of many pregnant women and their nurses and doctors.

REFERENCES

- Abel EL, Kruger M. 1998. What do physicians know and say about fetal alcohol syndrome? A survey of obstetricians, pediatricians and family medicine physicians. *Alcohol Clin Exp Res* 22:1951–1954.
- Astley SJ, Clarren SK. 1995. A fetal alcohol syndrome screening tool. *Alcohol Clin Exp Res* 19:1565–1571.
- Bearer C, Gould S, Emerson R, Kinnunen P, Cook CS. 1992. Fetal alcohol syndrome and fatty acid ethyl esters. *Pediatr Res* 31:492–495.
- Bradley K, Boyd-Wickizer J, Powell SH, Burman ML. 1998. Alcohol screening questionnaires in women: a critical review. *JAMA* 280:166–171.
- Clarren SK, Sampson PD, Larsen J, Donnell DJ, Barr HM, Bookstein FL, Martin DC, Streissguth AP. 1987. Facial effects of fetal alcohol exposure: assessment by photographs and morphometric analysis. *Am J Med Genet* 26:651–666.
- Ernhart CB, Morrow-Tlucack M, Sokol RJ, Martier S. 1988. Under-reporting of alcohol use in pregnancy. *Alcohol Clin Exp Res* 12:506–511.
- Ernhart CB, Green T, Sokol RJ, Martier S, Boyd TA, Ager J. 1995. Neonatal diagnosis of fetal alcohol syndrome: not necessarily a hopeless prognosis. *Alcohol Clin Exp Res* 19:1550–1557.
- Hall JG, Froster-Iskenius UG, Allanson JE. 1989. *Handbook of normal physical measurements*. New York: Oxford University Press. p 139, 189.
- Jacobson J, Jacobson SW, Sokol RJ, Martier SS, Ager JW, Shankanan S. 1994. Effects of alcohol use, smoking and illicit drug use on fetal growth in black infants. *J Pediatr* 124:757–764.
- Khoury MJ, Boyle C, DeCoufle P, Floyd L, Hymbaugh K. 1996. The interface between dysmorphology and epidemiology in the “diagnosis” and surveillance for fetal alcohol effects. *Pediatrics* 98:315–316.
- Larroque B, Kaminski M, Dehaene P, Subtil D, Delfosse MJ, Querleu D. 1995. Moderate prenatal alcohol exposure and psychomotor development at preschool age. *Am J Public Health* 85:1654–1661.
- Little BB, Snell LM, Rosenfeld CR, Gilstrap III LC, Gant NF. 1990. Failure to recognize fetal alcohol syndrome in newborn infants. *Am J Dis Child* 144:1142–1146.
- Morse BA, Weiner L. 1990. FAS: pediatric perspective and practice (poster). 5th Congress of the International Society for Biomedical Research on Alcoholism, Toronto.
- Morse BA, Idelson RK, Sachs WH, Weiner L, Kaplan LC. 1992. Pediatricians’ perspectives on fetal alcohol syndrome. *J Subst Abuse* 4:187–195.
- Nanson JL, Bolaria R, Snyder RE, Morse BA, Weiner L. 1995. Physician awareness of fetal alcohol syndrome: a survey of pediatricians and general practitioners. *CMAJ* 152:1071–1076.
- Sobell LC, Sobell MB. 1992. Timeline follow-back: a technique for assessing self-reported alcohol consumption. In: Litten RZ, Allen JP, editors. *Measuring alcohol consumption: psychosocial and biochemical methods*. Totowa, NJ: Humana Press. p 41–72.
- Stoler J. 1999. Reassessment of patients with diagnosis of fetal alcohol syndrome. *Pediatrics* 103:1313–1315.
- Stoler JM, Holmes LB. 1999. Under-recognition of prenatal alcohol effects in infants of known alcohol abusing women. *J Pediatr* 135:430–436.
- Stoler JM, Huntington KS, Peterson CM, Peterson KP, Daniel P, Aboagye KK, Lieberman E, Ryan L, Holmes LB. 1998. The prenatal detection of significant alcohol exposure with maternal blood markers. *J Pediatr* 133:346–352.
- Stratton K, Howe C, Battaglia F. 1996. *Fetal alcohol syndrome: diagnosis, epidemiology, prevention and treatment*. Washington, DC: National Academy Press. p 17–20.
- Streissguth AP, Barr HM, Sampson PD. 1990. Moderate prenatal alcohol exposure. Effects on child IQ and learning problems at age 7½ years. *Alcohol Clin Exp Res* 14:662–669.
- Streissguth AP, Kogan J, Bookstein FL, Barr H. 1996. *Understanding the occurrence of secondary disabilities in clients with fetal alcohol syndrome and fetal alcohol effects*. Seattle: University of Washington Press. p 4–8.
- Streissguth AP, Sampson PD, Barr HM. 1998. I.Q. at age 4 in relation to maternal alcohol use and smoking during pregnancy. *Dev Psychol* 25:3–11.