

Fetal Alcohol Syndrome

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PUBLIC HEALTH IMPORTANCE

Fetal alcohol exposure is an important cause of birth defects and central nervous system impairment including mental retardation, developmental delay, and other cognitive and behavioral abnormalities. Fetal alcohol syndrome (FAS) can be prevented by discouraging alcohol consumption during pregnancy or preventing pregnancy during periods of alcohol consumption.

For centuries researchers have observed associations between the alcoholism of parents and the growth and development of their children. Theories about etiology ranged from genetic causes to adverse environmental influences in the homes of alcoholic parents. The theory we now accept had its origins in France in the 1950s. In 1957, Heuyer et al. reported that children born to alcoholics had an excessive prevalence of neurological disorders as well as delayed growth and development (1). Christiaens et al. reported similar findings in 1960 (2). In 1968, Lemoine and colleagues described a pattern of abnormalities observed in the children of alcoholic mothers (3). In 1973, Jones and Smith observed the same pattern of abnormalities in Seattle, Washington, and coined the term fetal alcohol syndrome (4).

Published estimates of FAS prevalence range from 0.3 to 20 cases per 1,000 live births in various populations (5). Abel and Sokol reviewed studies of women in the United States, Canada, Australia, and several European countries during the 1970s and 1980s. Pooling the estimated cases in these various studies as well as the estimated total live births, they derived an overall rate of 1.9 cases of FAS per 1,000 live births. However, the studies used to generate

this estimate were biased in ascertainment for a number of reasons: 1) they were not population-based, 2) diagnosticians exhibited a degree of subjectivity in their diagnoses, and 3) varying methods of population selection and screening were used among the different racial and ethnic groups represented in the studies.

Abel and Sokol have recently reexamined the same literature and excluded studies that did not prospectively select consecutive pregnancies. As a result, they have lowered their revised estimate to 0.33 cases of FAS per 1,000 (6). Because this estimate was based on prospective studies only, does not include data on Native Americans, and is admittedly an underascertainment of the true prevalence of FAS, the commonly accepted estimate continues to be about 1 case per 1,000 births. Data comparing prevalence rates for this country and other countries are limited, but studies from European countries show rates of 1 to 2 cases per 1,000 live births (7).

Based on a birth prevalence estimate of 0.33 cases per 1,000, the annual financial burden of FAS in the United States is estimated to be \$74.6 million (6). Approximately 78% of this amount is attributed to costs associated with mental retardation and low birth weight. Mental retardation is believed to be present in about 53% of FAS cases. The fact that these estimates were based on cases of FAS only is noteworthy. If we assessed all other documented

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alcohol-related effects—low birth weight, specific birth defects, and other cognitive and behavioral disorders—the costs would be much higher.

The surveillance of FAS is the foundation for assessing trends in occurrence and in planning and evaluating prevention activities. Reducing FAS and increasing the number of women who abstain from drinking during pregnancy are among the maternal and infant health objectives for the year 2000 (8). To establish these objectives, the U.S. Department of Health and Human Services used baseline data for FAS rates from the Birth Defects Monitoring Program (BDMP) and baseline rates for alcohol use in pregnancy from the 1988 National Maternal and Infant Health Survey (NMIHS). In addition, state health departments were mandated to monitor and report annually the proportion of infants born with FAS. For additional information about related topics and surveillance activities, see the Behavioral Risk Factors Before and During Pregnancy, Pregnancy-Related Nutrition, Low Birth Weight and Intrauterine Growth Retardation, and Prevalence of Birth Defects chapters.

HISTORY OF DATA COLLECTION

Although FAS has been recognized as a clinical entity in the United States since 1973, no surveillance system has been designed expressly to monitor its occurrence. CDC has, however, conducted surveillance for birth defects for 25 years through the Metropolitan Atlanta Congenital Defects Program (MACDP) and the national BDMP. The MACDP, begun in 1967, is the oldest active birth defects surveillance system in the United States and is the prototype for many developing state systems. The BDMP, CDC's nationwide birth defects surveillance system, has been in operation since 1974. These two systems were designed primarily to monitor major congenital defects in infants; they were not designed to address some of the more specific problems encountered in tracking syndromes, such as FAS, that have less distinct anomalies associated with the syndrome.

Surveillance efforts have improved over the past 15 years because of the evolution of the case definition and designation of an *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* code that can be used for FAS (9). In 1980, an FAS case definition was accepted by the Fetal Alcohol Study Group of the Research Society on Alcoholism (10). With some modification, the definition was updated in 1989 to specify that a child must manifest signs of abnormality in each of the following categories to have a secure diagnosis (11):

- Prenatal and/or postnatal growth retardation (weight and/or length or height below the 10th percentile when corrected for gestational age).
- Central nervous system involvement including neurological abnormality, developmental delay, behavioral dysfunction or deficit, intellectual impairment, and/or structural abnormalities such as microcephaly (head circumference below the third percentile) or brain malformations found on imaging studies or autopsy.
- A characteristic face, currently qualitatively described as having short palpebral fissures, an elongated midface, a long and flattened philtrum, thin upper lip, and flattened maxilla.

Fetal alcohol effects (FAE) is frequently used to designate children with milder or less complete manifestations of fetal alcohol impairment not meeting a full FAS definition. This term is used when alcohol exposure during pregnancy has been documented. It is a controversial term with a less clear definition than the definition for FAS.

The complexity of the FAS case definition, the variability of physical expression at birth, and the enhancement of diagnosis with age are features of FAS that have posed serious challenges for complete case ascertainment in birth defects surveillance systems that focus case-finding in the neonatal and infancy periods. Nevertheless, birth defects surveillance systems can identify

and track those infants for which manifestations of FAS are evident in the neonatal period.

CDC SURVEILLANCE ACTIVITIES

Birth Defects Monitoring Program

The BDMP collects data on births occurring in some 1,200 community hospitals throughout the country; hospital participation is voluntary. Because the birth data are obtained from a non-random sample of U.S. hospitals, BDMP birth data are not population-based and do not constitute a random sample of all U.S. births. For a detailed description of the BDMP, see the Prevalence of Birth Defects chapter.

The surveillance of FAS was influenced by the 1979 publication of the *ICD-9-CM*—the first revision of the coding scheme since the recognition of FAS as a clinical entity in the United States (9). In this newest revision, an *ICD-9-CM* code that includes FAS was first assigned. Because BDMP coding is based on this scheme, the program began in 1979 collecting information on infants assigned this code during the newborn period. Since then, the BDMP has accumulated almost 15 years of national data on infants diagnosed at birth as having FAS.

Metropolitan Atlanta Congenital Defects Program

The MACDP, CDC's population-based birth defects surveillance system, monitors all births occurring in the five-county metropolitan Atlanta area—approximately 38,000 births each year. In the 25 years that the MACDP has been in operation, it has monitored >700,000 births. The MACDP includes information on all live-born and stillborn infants with a diagnosis of at least one major birth defect within the first year of life; diagnoses continue to be ascertained on these infants up until the sixth birthday. For a detailed description of the MACDP, see the Prevalence of Birth Defects chapter.

For 20 years, CDC has tracked trends for infants affected with FAS. In 1974, 1 year after FAS was recognized in the United States as a

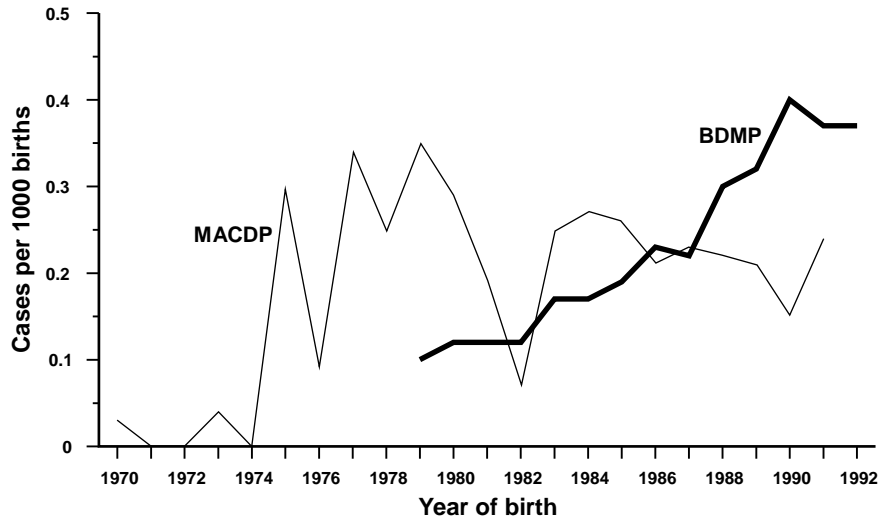
clinical entity, FAS was added to the list of defects monitored by the MACDP. Because the coding system for MACDP is a specific modification of the *ICD-9-CM* and the British Pediatric Association coding schemes for use with birth defects surveillance systems, coding for FAS was structured more definitively than coding used in the BDMP. In the MACDP, FAS has its own unique code (760.710), distinguishable from the code for **probable** FAS (760.718), which may also include FAS facies.

GENERAL FINDINGS

Even though the BDMP and MACDP have differed considerably in ascertainment methods, geographic focuses, and periods monitored, they have produced very similar crude FAS prevalence estimates for infants in the first year of life. Between 1979 and 1992, the BDMP generated an overall prevalence estimate of 0.2 cases per 1,000 births. Between 1974 and 1991, the MACDP generated a birth prevalence estimate of 0.2 cases per 1,000 live births for FAS (codes 760.710 and 760.718), an estimated prevalence of 0.1 cases per 1,000 live births for **definitive** FAS (code 760.710), and an estimated prevalence of 0.08 cases per 1,000 live births for **probable** FAS (code 760.718). We suspect that the estimates from both systems underestimate the true prevalence for FAS because they are based on the recognition and diagnosis of FAS in infancy. Many FAS researchers believe that the clinical features of this syndrome become more prominent as a child ages, suggesting that more cases would be identified beyond the birth and infancy periods and that recognition in the newborn period is difficult at best.

Even though the two systems give the same overall estimate of the prevalence of FAS, they give a different sense of trends over the period monitored (Figure 1). The estimated prevalence of FAS among newborns identified through the BDMP has increased from 0.1 cases per 1,000 births in 1979 to 0.4 cases per 1,000 in 1992 (chi-square test for linear trend = 346.4, $p < 0$). Rates calculated from MACDP data are not stable from year to year and do not show a trend during the same period. This instability may be

FIGURE 1. Prevalence of fetal alcohol syndrome — Birth Defects Monitoring Program (BDMP) and Metropolitan Atlanta Congenital Defects Program (MACDP), 1970–1992



a function of the smaller number of births followed by the MACDP. Given the increased awareness of FAS among health-care providers during the last decade, we have difficulty determining whether the statistically significant increase in prevalence shown in BDMP data represents a true increase in prevalence or whether it reflects the role that increased awareness might play in identifying an increasing proportion of the cases in a population with an essentially stable attack rate.

Serdula et al. (12) report that between 1985 and 1988, the percentage of women who drank during pregnancy declined, but this decline was not evident for less educated and younger women. Moreover, for women who did drink during pregnancy, the median number of drinks remained the same during this 4-year period. Even though we have background information on alcohol exposure in the population of interest, we do not have comparable population-based data on FAS outcome. Therefore, it is difficult to predict whether the true prevalence of FAS might be stable, decreasing, or increasing over the period. Reports suggest that FAS prevalence is underascertained by a wide margin, particularly in the newborn period (13). If

this is true, increasing ascertainment could easily produce a spurious trend estimate. Analyzing trends by racial and ethnic groups might be instructive.

BDMP data show FAS to be a widespread problem in the U.S. population (Table 1); racial and ethnic differences may be related to economic, social, and additional factors other than race per se. In the BDMP and MACDP, the number of cases per group has been small enough each year to compromise the validity of stratified trend estimates. Even though rates vary considerably by race and ethnicity, the burden of the disease affects all groups. For example, whites exhibit a lower prevalence (0.11 cases per 1,000 births) than other racial and ethnic groups. However, because whites account for more than three fourths of all U.S. births, roughly a third of FAS births are white. Compared with rates for other groups, rates among both Native Americans and blacks are quite high; nevertheless, the overall public health burden is quite different for the two groups because Native American births represent about 1% of all U.S. births, and black births represent >15% of all U.S. births.

TABLE 1. Prevalence of fetal alcohol syndrome (FAS) by race/ethnicity — Birth Defects Monitoring Program (BDMP), 1981–1991

	FAS cases		BDMP births (in 1,000s)		Prevalence per 10,000
	N	(%)	N	(%)	
Black	710	(47.0)	873	(12.4)	8.1
White	537	(35.6)	4,887	(69.2)	1.1
Native American	77	(5.1)	25	(0.4)	31.0
Hispanic	45	(3.0)	382	(5.4)	1.2
Asian	3	(0.2)	101	(1.4)	0.3
Other	137	(9.1)	791	(11.2)	1.7
Overall	1,509	(100.0)	7,059	(100.0)	2.1

INTERPRETATION ISSUES

Problems in Identifying FAS

CDC's goal is to improve FAS surveillance methods in order to determine the scope of the problem and better serve prevention efforts. Successful, sound surveillance of FAS depends on accurate clinical diagnosis and more generally on a clearly understood and commonly accepted case definition that can be arrived at easily by clinicians. FAS does not conform to this requirement.

First, the diagnosis of FAS is difficult and subjective. Because we have no invariable core of specific features that designates a case patient, the diagnosis depends on FAS dysmorphology expertise to make the judgment, given some objective findings and a subjective impression.

Second, some FAS experts have said that ages 3–8 years are the best times for recognition because the distinct pattern of FAS facial abnormalities is fully expressed at these ages. Further, cognitive and behavioral delays manifest themselves at these ages when FAS children fail to perform developmental skills (e.g., kindergarten readiness at 4 years and reading and math skills at 7 years). However, no screening methods have been developed for this age-group, and identifying a single capture point for surveillance

is difficult. Birth defects surveillance systems capture diagnoses made during infancy, sometimes only during the early neonatal period, a time when the diagnosis is particularly difficult.

Finally, numerous sources of biases are inherent in the case ascertainment process. For example, practical diagnosis depends on knowledge of the mother's alcohol consumption during pregnancy. Many, if not most, clinicians are reluctant to make a diagnosis without this knowledge. Dependence on alcohol exposure information creates a tautological relationship between the exposure and the outcome, increasing the potential for biased judgments in a diagnostic setting already subject to bias.

Another possible source of bias in FAS diagnosis is reflected in the 1975–1992 MACDP data, which revealed 76 FAS diagnoses at Hospital A, a large inner-city public and teaching hospital serving poor women, most of whom are black, and only two FAS diagnoses at Hospital B, a large suburban hospital serving affluent women, most of whom are white. Interpreting this large discrepancy in rates between two different populations is difficult. Do women who deliver at Hospital B drink less than those at Hospital A? Do environmental factors such as nutrition and smoking influence outcome? Are clinicians at Hospital A more willing than those at Hospital B to elicit the history of alcohol consumption in pregnancy, to make the diagnosis,

and to record it in the chart? Are clinicians at Hospital A more knowledgeable about FAS and therefore more confident about making the diagnosis because they are in a teaching hospital and because there is an FAS research presence there? Perhaps children born at Hospital A are more likely to be followed at Hospital A outpatient departments if they have medical problems because they are less likely to have private pediatricians than children born at Hospital B. FAS may be overdiagnosed in some hospitals and underdiagnosed in others, but it is generally believed to be underascertained nationally. One report revealed that the MACDP failed to capture approximately 30% of cases of FAS that were diagnosed by other sources in infancy and early childhood (*Cordero J, Tosca M, unpublished data, 1993*).

FAS surveillance differs from the traditional surveillance approaches that have worked so well for infectious diseases and major congenital malformations. Even the best active birth defects surveillance systems such as the MACDP cannot be expected to capture FAS well without major modifications because of the subjectivity and the timing of the diagnosis, the lack of widespread FAS diagnostic expertise, and questionable tendencies toward social class and racial and ethnic biases in case ascertainment. Factors such as these are important to consider when interpreting FAS rates and designing methods for FAS ascertainment. To improve surveillance, we need to focus on four goals: 1) developing a more specific and objective case definition, 2) developing better age-specific screening and diagnostic methods, 3) training physicians and health-care providers to accurately screen and diagnose FAS, and 4) creating state and national systems for aggregating FAS data from a variety of sources.

Alternative Systems of Case Ascertainment

CDC provides both financial and technical support to state health departments and universities in an effort to establish affordable and efficient methods for estimating the prevalence of fetal alcohol syndrome. Cooperative agreements with these agencies and institutions support the in-

vestigation of clinic-, school-, and social services-based approaches to FAS case ascertainment. The state of Washington is piloting a school-based program to screen all students in grade 1 by using a two-tier approach. Children are first screened on the basis of growth parameters and facial malformations; they are then referred to a special diagnostic clinic for examination by a dysmorphologist. Missouri is designing a case-finding system to refer all children removed from the home by protective services to a physician for a medical examination, which will include FAS assessment. In addition, the University of New Mexico is conducting population-based FAS diagnostic clinics patterned after a project that was conducted in the early 1980s among Native American communities.

A final methodology, which has been derived by CDC scientists working in Alaska, involves cross-linkage of existing data sets containing FAS diagnostic information. Data from birth certificates, death certificates, Medicaid, the Indian Health Service, and private physician practices were used to derive prevalence estimates for native populations (14). This approach provides a low-cost strategy for capturing cases that may be missed by surveillance systems that monitor rates among newborns only.

EXAMPLES OF USING DATA

In 1991, CDC entered into an agreement with the Indian Health Service and Alaska to provide epidemiologic assistance in determining the prevalence of FAS among all racial and ethnic groups in the state and to assist in the design of FAS prevention and evaluation activities. An FAS case file was developed to serve as the basis for a preliminary estimate of the prevalence rate of FAS among Alaska Native women. Earlier efforts at determining prevalence had been nonsystematic and biased in the ascertainment process. Relevant data from Indian Health Service data files and state files were cross-linked to produce an unduplicated number of FAS cases. Next, medical records were abstracted to confirm the presence of FAS. Using live births per year for the birth years of cases identified, researchers established a preliminary estimate of 2.1 cases of FAS per 1,000

live births (14). This estimate was believed to be an underascertainment of the true prevalence because of the very stringent case definition used and because of certain inherent methodologic constraints (underreporting in medical charts, unavailability of medical charts, and lack of access to all cases diagnosed by private physicians). Continued efforts are being made to increase ascertainment in order to generate more reliable estimates for all racial and ethnic groups in the state. These estimates will be used to justify the need to expend resources on prevention efforts and to explore the use of this methodology for tracking the effects of past and ongoing prevention efforts.

In 1983, May et al. published the results of an extensive effort to determine the prevalence of FAS among Southwestern Indians (15). The method used for case finding in this study was to go into a community and organize diagnostic clinics aimed at identifying children with FAS. Community preparation and the education of providers were key elements of the success of this approach, which resulted in what remains to date the most reliable estimates of FAS among this population. In 1993, the University of New Mexico was funded by CDC to replicate this model statewide to determine the feasibility of using this approach on a population basis to determine prevalence rates of all racial and ethnic groups. This methodology could provide yet another alternative to determining prevalence rates for FAS.

In 1991, Oklahoma analyzed data from its Pregnancy Risk Assessment and Monitoring System and found that 12% of pregnant women in Oklahoma consumed a median of 8.2 alcoholic beverages per month during pregnancy. Using this and other information, the state developed an FAS Prevention Cooperative Agreement proposal, funded by CDC. Their project identified college-educated women as a targeted group for prevention activities. Further efforts are being developed to determine the level of drinking among this group, and early intervention approaches are being explored among college-aged men and women on one university campus in the state. The state is also exploring the surveillance of newborns and the

feasibility of a cross-linkage project similar to that done by Alaska.

FUTURE ISSUES

BDMP data will be used to monitor our progress in meeting the year 2000 national health objective for the reduction of FAS (8). Current trends indicate an increase in FAS that relates in part to increased awareness and recognition of the syndrome (13). Reaching a national rate of 0.12 cases per 1,000 live births over the next 6 years, given our current rate of 0.40 cases per 1,000 live births, will be a challenge. Further, we must consider the need to monitor the occurrence of other alcohol-related birth disorders. Facial malformations and central nervous system deficits that are characteristic of FAS have been noted among children whose symptoms do not meet the full case definition of FAS as defined by the Alcohol Working Group of the Society for Research on Alcoholism. The practice of assigning a diagnosis of fetal alcohol effects to these milder alcohol-related conditions has been discouraged by the working group (11). The working group recommends the use of the term **alcohol-related birth defects** to “connote attribution of an observed anatomic or functional outcome to the impact of alcohol on the offspring,” but it does not offer a case definition (11). Thus, a fundamental measurement problem exists because we have no case definition for children affected by in utero exposure other than those who have full-blown FAS. Future progress in surveillance will require a more concise case definition of FAS as well as a case definition for alcohol-related birth disorders.

The lack of precision in definition relates to two other important concerns in FAS surveillance—biased ascertainment and misclassification. In the Alaska study, potential cases of FAS were identified from major health data sets and were confirmed by in-depth medical chart review by using a case definition developed for the study (14). In that process, we discovered that only 14 of the 53 cases abstracted met the case definition for FAS. Documentation of alcohol exposure was present in 44 of the 53 potential

cases given the *ICD-9-CM* code for FAS, which may be evidence of a lack of specificity of the code. The paucity of population-based prevalence data has contributed to biases among clinicians and health officials in recognizing the potential problems of FAS among persons of all socioeconomic statuses, races, and ethnicities. Therefore, in the future, we must expand surveillance systems to include population-based, systematic methods of identifying children with FAS at ages that optimize correct diagnoses.

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