1

Prenatal Alcohol Exposure, FAS, and FASD: An Introduction

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1.1

Introduction

Prenatal Alcohol Exposure (PAE) can result in a wide range of physical, psychological, behavioral, and social problems that affect the individuals, their families, and their communities. Indeed, PAE is a major public health issue placing undue burden on all aspects of society. Among the most severe outcomes of PAE is the Fetal Alcohol Syndrome (FAS), which is characterized by growth deficits, facial anomalies, and neurobehavioral problems. However, FAS is not the only detrimental outcome of heavy gestational alcohol exposure, and the majority of individuals affected by such exposure do not meet the diagnostic criteria of FAS. Currently, PAE is increasingly understood as the cause of a continuum of effects across many domains. Fetal Alcohol Spectrum Disorder (FASD) is a nondiagnostic term used to identify the wide array of outcomes resulting from prenatal exposure to alcohol. These outcomes range from isolated organ damage or subtle developmental disabilities to stillbirths and FAS. Perhaps the most pervasive outcome following prenatal alcohol exposure is what is now commonly referred to as an Alcohol-Related Neurodevelopmental Disorder (ARND). While individuals with ARND may exhibit many of the alcohol-related brain and behavioral abnormalities of FAS, they may not display the characteristic facial dysmorphia required for an FAS diagnosis. Although cases of FASD are often not as easily recognized as FAS, they can be just as serious. Unfortunately, missed diagnoses of FASD can have devastating consequences, placing heavy emotional, financial and social stresses on the individual and all parties involved (Riley and McGee, 2005).

Although the relationship between alcohol consumption during pregnancy and abnormal fetal development has been alluded to throughout history (Warren and Hewitt, 2009), FAS went unrecognized until the late 1960s and early 1970s (Lemoine et al., 1968; Jones and Smith, 1973; Jones et al., 1973). Since those initial defining case studies, the scientific literature on the effects of PAE on the developing fetus has grown rapidly. A simple search of pubmed.gov (U.S. National Library of Medicine) using “fetal alcohol syndrome” as a search term turned up almost 3500 citations. This research has improved our understanding of the relationship...
between alcohol exposure and developmental deficits, and has resulted in an increased social awareness of the risks of drinking during pregnancy, prevention efforts to reduce these risks, and development of intervention programs to help promote positive outcomes for individuals with FASD. However, despite our current knowledge and the progress that has been made, many challenges remain in understanding how alcohol exerts its effects, in developing efficacious and effective prevention and intervention programs, and how best to improve the daily functioning of these individuals.

1.2 History

It has been suggested that the adverse effects of alcohol on the developing fetus have been recognized for centuries. Some of the earliest references date back to Greek and Roman mythology and Judeo-Christian tradition, such as the ancient Carthaginian custom that forbade bridal couples from drinking wine on their wedding night, and the belief that alcohol consumption at the time of procreation leads to the birth of defective children (Jones and Smith, 1973). Passages in Robert Burton’s *The Anatomy of Melancholy* allegedly quote Aristotle describing an association between alcoholic mothers and disabled children in *Problemata*: “…foolish, drunken and harebrained women [for the] most part bring forth children like unto themselves, morose and languid” (Burton, 1621). However, there remains much controversy regarding the validity of these claims and sources. Although many authors have assumed Burton to be quoting Aristotle’s words verbatim, there is no evidence of any such statement in *Problemata*, nor in any of Aristotle’s other works (Abel, 1999). Others have claimed that the Carthaginians did not truly understand that drinking during pregnancy caused problems; rather, they believed that intoxication at the exact moment of conception led to the birth of a deformed offspring (Calhoun and Warren, 2007).

More recent and credible historical reports, however, have documented alcohol’s teratogenic effect. During the 1700s, a group of English physicians described children born to alcoholic mothers as “weak, feeble, and distempered” (Royal College of Physicians of London, 1726). A deputy medical officer of the Convict Prison in Parkhurst, England, noticed that imprisoned pregnant alcoholic women had high rates of miscarriage, and that those offspring which survived displayed distinctive patterns of birth defects (Sullivan, 1899). From these observations, Sullivan concluded that alcohol had a direct effect on the developing embryo.

Despite these observations and early animal studies supporting an association between gestational alcohol exposure and adverse outcomes (e.g., Stockard, 1910), the first clinical accounts of alcohol’s teratogenic effects were not published until the late 1960s. In 1968, Lemoine and colleagues published their report entitled “Outcome of children of alcoholic mothers” (Lemoine et al., 1968), which established a connection between maternal alcohol consumption during pregnancy and abnormal fetal development, describing common problems of children born to
1.3 Diagnosing the Effects of Prenatal Alcohol Exposure

1.3.1 Fetal Alcohol Syndrome

There are several suggested diagnostic schemas for FAS (e.g., Bertrand et al., 2004; Chudley et al., 2005; Hoyme, 2005) and, while there are minor differences between them, all require anomalies in three distinct areas: (i) prenatal and postnatal growth deficits; (ii) facial dysmorphology; and (iii) central nervous system (CNS) dysfunction. Typically, growth retardation is defined as evidence of prenatal or postnatal weight or height at or below the 10th percentile, after correcting for age, gender, race, and other appropriate variables. The Canadian guidelines also recommend evidence of a disproportionately low weight-to-height ratio at or below the 10th percentile. Most guidelines recommend three essential dysmorphic features—a smooth philtrum, a thin upper vermillion border, and small palpebral fissures—although the revised Institute of Medicine (IOM) guideline requires only two of the three characteristics (Hoyme et al., 2005). Finally, a diagnosis of FAS requires evidence of CNS abnormality. Within this criterion, the diagnostic schemas differ more substantially. For example, the revised IOM guideline only requires evidence of structural brain abnormalities, such as diminished head circumference at or below the 10th percentile. The CDC criteria are more extensive, outlining structural, neurological, and functional CNS dysfunction. Structural anomalies may be evidenced by the two criteria delineated in the IOM guidelines, as well as brain abnormalities observed with neuroimaging techniques. Seizures or other signs of neurological damage not attributable to postnatal insult may qualify as evidence of neurological problems. Lastly, functional abnormalities are defined as a global cognitive deficit (such as a decreased IQ), or deficits in three different functional CNS domains, which include cognition, behavior, executive functioning, and motor functioning. The Canadian guidelines outline eight domains that must be assessed: hard and soft neurologic signs; brain structure; cognition; communication; academic achievement; memory; executive functioning and abstract reasoning; and attention deficit/hyperactivity. Diagnosis requires evidence of impairment in three of these domains.
1.3.2 Fetal Alcohol Spectrum Disorder(s)

It is now recognized that there is a spectrum of deficits arising from PAE; FASD is the umbrella term used to describe this broad range of outcomes. Since the term FASD is not diagnostic, some of the guidelines (Chudley et al., 2005; Hoyme et al., 2005) use the terms ARND or ABRD (alcohol-related birth defect) to describe these FASDs. ARBD is a term which refers to individuals with a confirmed history of PAE and who display congenital birth defects, such as physical malformations or organ abnormalities. The ARND classification refers to individuals with a confirmed history of PAE who have behavioral and cognitive deficits related to CNS dysfunction. For example, an association between maternal alcohol use and sudden infant death syndrome (SIDS) has been suggested (e.g., Burd and Wilson, 2004). This would make SIDS an FASD in those cases where PAE was suspected, if other causes could be ruled out. Similarly, an increased risk of congenital heart defects has been associated with prenatal alcohol exposure; thus, such heart defects might be considered an FASD/ARBD if the mother drank heavily during pregnancy. Behavioral problems in children exposed to alcohol in utero, but who do not meet the diagnostic criteria of FAS, are perhaps the most commonly cited type of FASD/ARND.

1.4 Risk factors influencing FAS and FASD Conditions

The variation in the range of phenotypes of individuals with PAE suggests that alcohol’s teratogenic effects can be moderated or exacerbated by other variables. Not every woman who drinks heavily during pregnancy will give birth to a child with an FASD (Warren and Foudin, 2001), and not all children with an FASD have the same deficits (Bertrand et al., 2004). In fact, there have been reports of discordance among twin pairs in regards to FAS (Warren and Li, 2005; Streissguth and Dehaene, 1993). Numerous biological and environmental factors have been shown to influence the effects of alcohol on the developing fetus, with the most obvious and important factors being those related to the nature of the PAE. The amount of alcohol consumed is highly correlated with the severity of outcome; typically, a higher level of alcohol consumption, along with longer duration of exposure, will generally lead to more adverse effects (Bonthius and West, 1988; Maier, Chen, and West, 1996). However, a linear relationship between dosage and severity may not always be expected. Studies in both animals and humans have revealed that the pattern of alcohol consumption may moderate dose effects. A binge-like exposure results in more severe neuropathology and behavioral alterations than does chronic exposure (Bonthius, Goodlett, and West, 1988), and those women who binge drink are at a higher risk of having a child with neurobehavioral deficits than those who drink chronically during pregnancy (Maier and West, 2001). In fact, Jacobson et al. (1998) have proposed that describing consumption by the average number of drinks per occasion is more useful in predicting outcome than
the average number of drinks per week. A high peak blood alcohol concentration induced during binge episodes appears to be a significant risk factor for prenatal injury (Streissguth et al., 1993; Warren and Foudin, 2001).

Phenotype can also differ as a function of the developmental timing of alcohol exposure. For example, exposure during different critical periods of development will strongly influence not only the specific systems affected but also the severity of the deficit, as different organ systems develop at different rates and times during gestation. The clearest example of this “critical period” relates to the facial features required for a diagnosis of FAS. Studies in mice have shown the dysmorphic facies to be a result of alcohol exposure during a limited period of gestation, the human equivalent of which would be gestation weeks 3 and 4 (Sulik, 2005). Alcohol exposure during the first trimester interferes with the proliferation, migration, and differentiation of precursor cells in the cerebral cortex (Cook, Keiner, and Yen, 1990; Miller, 1993; Miller, 1996); however, exposures at other times might have other effects, such as altered synapse formation or changes in myelination. Alcohol exposure during the third trimester interferes with the development of specific brain structures, including the hippocampus, cerebellum, and prefrontal cortex (Livy et al., 2003; Maier et al., 1999; Maier, Miller, and West, 1999). Thus, alcohol’s teratogenicity interferes with various ontogenetic stages of neural development. Consequently, the pattern of structural and functional abnormalities will vary depending on alcohol exposure during particular critical periods of development, as different aspects of the developing nervous system become more or less vulnerable to alcohol’s toxicity.

The genetic background of both the mother and fetus is another important factor that influences the effect of alcohol on the developing fetus. Genes affect the metabolism of alcohol and an organism’s functional sensitivity to alcohol. For example, particular alleles for alcohol dehydrogenase (ADH1B*2 and ADH1B*3) allow for a faster alcohol metabolism, thereby reducing the risk of exposure to the fetus (McCarver et al., 1997).

Environmental factors related to prenatal care and nutrition are also important risk modifiers in FASD. Many mothers who drink during pregnancy do not receive proper prenatal care and nutrition. A complex interaction exists between nutrition and alcohol: food affects the rate of alcohol absorption and metabolism (Sedman et al., 1976), but alcohol often alters the requirement for and absorption of nutrients (Morgan and Levine, 1988). Alcohol exposure in combination with low nutrient levels increases the risk for FASD. Other risk factors for FASD include polysubstance abuse, maternal age, ethnicity, and socioeconomic status (Warren and Foudin, 2001).

1.5 Prevalence and Impact of FAS and FASD

Unfortunately, the prevalence of FAS and FASD is not as well understood as might be hoped. Today, epidemiological research into FAS and FASD is constantly challenged by issues related to methodology and questions regarding the diagnostic
criteria used (May and Gossage, 2001). In the United States, the overall estimated prevalence of FAS is approximately 0.5 to 2 per 1000 births (May and Gossage, 2001), although within certain groups the prevalence is estimated to be much higher. For example, among the Plain and Plateau culture tribes in the United States, the average FAS rate is 9 per 1000 children between the ages of one and four years (May, McCloskey, and Gossage, 2002). Elsewhere, rates among the Southwestern tribes varied from 0.0 to 26.7 per 1000 over the time period of 1969–1982, depending on the specific community studied (May et al., 1983). These high-risk communities are typically of low socioeconomic status, and include a significant proportion of individuals who binge-drink on a frequent basis. The rate of FAS in children aged between five and nine years in the Cape Colored community of the Western Cape Province of South Africa is proposed to be as high as 46.4 per 1000 (May et al., 2000), while Canadian FAS data have estimated a range of prevalence which varies from 0.52 to 14.8 per 1000 (Habbick et al., 1996, Williams, Odaibo, and McGee, 1999). In one county in Washington, USA, the number of first graders with FAS was reported as 3.1 per 1000 (Clarren et al., 2001).

When considering the entire range of prenatal alcohol effects, the incidence of FASD has been estimated to be 9.1 per 1000 births (Sampson et al., 1997), which is approximately one out of every 100 births (May and Gossage, 2001). Health Canada has estimated the incidence of FASD at 9 per 1000 births (Health Canada, 2006).

Perhaps one of the most important rates that must be addressed is the prevalence of FAS in families who already have a child with FAS. Women who have already given birth to a child with FAS are at extremely high-risk of having another affected child if they continue to abuse alcohol, and typically later-born children are more impacted than the older children in the family.

Given these numbers, it is not surprising that FASD is associated with significant social and economic ramifications. FASD can cause long-lasting medical and psychological problems, and result in economic costs of billions of dollars. Moreover, individuals with FASD suffer from many physical, mental, behavioral, and educational problems which affect daily functioning and have lifelong implications. As a result, individuals with FASD often experience mental health issues, problems in school and work environments, trouble with the law, substance abuse, inappropriate sexual behavior, and difficulties with independent living, among other challenges (Bertrand et al., 2004; Streissguth et al., 2004).

Lupton, Burd, and Harwood (2004) have approximated the cost of a single individual with FASD to be US$2.0 million throughout the individual’s lifetime. More recently, the US National Task Force on FAS estimated the adjusted annual cost of FAS in the US to be approximately US$3.6 billion (Olson et al., 2009). Moreover, as the cost of medical treatment, special education, psychosocial intervention and residential care for individuals with FASD increases, these costs will only continue to rise (Lupton, Burd, and Harwood, 2004). In Canada, the average annual cost per child with FASD in 2009 was estimated at $21,642, with the total annual cost of FASD being $5.3 billion (Stade et al., 2009).
Given the incredible impact of FAS/FASD on both individuals and society as a whole, the prevention of PAE and its effects is crucial. Despite ongoing health warnings, pregnant women continue to use alcohol, particularly in patterns that significantly increase the risk of prenatal injury. In 2004, the Center for Disease Control (CDC) reported that 13% of women in the US continue to use alcohol even after knowledge of their pregnancy, and 3% report binge drinking and/or drinking at levels that are known to produce adverse effects in the developing fetus (Bertrand et al., 2004). Furthermore, approximately 55% of women of childbearing age in the US report drinking alcohol, and 12.4% report binge drinking (Rasmussen et al., 2009). As over 50% of pregnancies in the US are unplanned (Finer and Henshaw, 2006), these women are particularly high-risk. Unaware of their pregnancies, women will likely continue their alcohol use during the early stages of embryonic development. These data suggest that more effort must be made to develop effective, evidence-based prevention strategies to reduce the number of alcohol-exposed pregnancies. The first step of prevention must address the disparity between knowledge and behavior, understanding why some women—despite being aware of FAS—continue to engage in high-risk drinking behaviors.

Different levels of prevention fall along a continuum ranging from universal to selective to indicated intervention; as risk behaviors increase, prevention measures become more targeted and intensive (Barry et al., 2009).

Universal prevention attempts to promote the health of the general public, targeting all members of a population or particular group, regardless of risk. Examples of universal approaches include encouraging the abstinence from alcohol during pregnancy, raising public awareness of FASD, and creating alcohol policy and educational programs that minimize the risks of alcohol consumption during pregnancy. Methods to disseminate information include media campaigns, educational materials, and alcoholic beverage labeling. Research into the impact of the U.S. Federal Beverage Labeling Act in several different populations, including a sample of inner-city African-American pregnant women (Hankin et al., 1996; Hankin et al., 1993; Hankin, Sloan, and Sokol, 1998), has revealed an increased awareness of alcohol beverage warning labels since the law’s inception in 1989. However, despite this increasing awareness, drinking rates have not necessarily followed suit. Within this sample, Hankin et al. (1993) observed a slight decrease in alcohol consumption, although the decline was apparent only among lighter drinkers; the warning labels did not have any significant effect on high-risk drinkers (Hankin et al., 1993). Furthermore, whilst there was a significant decrease in drinking behaviors post-label for women who had not previously given birth, no change was evident for those women who had already given birth to a child (Hankin et al., 1996). Ultimately, the observed decrease in drinking rates appears to be only short-lasting, and the effectiveness of the labels may lose their impact as women become habituated to them (Hankin, Sloan, and Sokol, 1998).
associated with alcohol consumption during pregnancy, insufficient data are available regarding any concrete changes in drinking rates among pregnant or non-pregnant women of childbearing age (Barry et al., 2009).

Selective prevention is directed at individuals who are at greater risk than the rest of the general public of having an alcohol-exposed pregnancy due to risky behaviors, such as women of childbearing age who consume high levels of alcohol. Selective interventions are more specific when compared to universal preventions, and may include outreach to at-risk groups, alcohol screening at doctors’ offices, referral, and brief intervention strategies aimed at reducing the mother’s drinking and minimizing harm to her potential offspring.

Indicated preventions are aimed specifically at the highest risk individuals, such as binge-drinkers, women who are alcoholics, and women who have already given birth to a child with an FASD. These approaches involve a screening process to identify such individuals and help them minimize or cease their alcohol abuse. Several brief screening instruments have been developed for use in a diversity of populations to identify problematic alcohol use in women (Bertrand et al., 2004). Studies have documented the efficacy of screening and brief interventions in reducing risky drinking behaviors and alcohol-exposed pregnancies (Floyd et al., 2009). These brief interventions include clinical advice and counseling regarding the risks of PAE, encouragement to change behaviors, and strategies and goals for reducing the use of alcohol during pregnancy.

1.7 Interventions

The considerable variability in the type and extent of deficits of FASD has led to the development of efficacious interventions becoming a particular challenge. A diagnosis of FAS or the identification of an FASD does not lend itself to a single effective treatment practice that could target the entire range of neurobehavioral problems which an individual may have (Hannigan and Berman, 2000). The various combinations of physical, mental, behavioral, and learning/educational problems among individuals with PAE highlight the complexity of these disorders, and the necessity for interventions that are problem-specific as well as flexible. Rather than confront the entire scope of the disorder—which may be overwhelming and unfeasible—specific behavioral problems should be identified in order to direct specific treatments (Hannigan and Berman, 2000). For example, recent research into interventions for FASD has demonstrated the efficacy of targeted treatments for social skills impairment associated with prenatal alcohol exposure (Paley and O’Connor, 2009).

In addition to intervening with alcohol-exposed individuals to mitigate the deficits and consequences of PAE, treatment practices should focus on providing education and support to the families and caregivers of these individuals. The consequences of FASD extend far beyond the experiences of affected individuals. Both biological and foster parents often experience high levels of stress associated
with dealing with their child’s impairments (Paley et al., 2006). Many foster parents have expressed their need for more education about FASD, parenting skills training, social support, and professional services to help raise a child with alcohol-related disabilities (Brown, Sigvaldason, and Bednar, 2004). In fact, it has been shown that educating parents and caregivers to realize that the origins of their child’s behavioral problems are rooted in brain changes may help them become more understanding and respond to their child in a more supportive manner (Paley and O’Connor, 2009). Interventions should address the issues of the families of those affected by PAE in order to improve their own adjustment and functioning, as well as that of their child.

Current research supports the efficacy of numerous treatment approaches for individuals with FASD as well as their caregivers (as reviewed in Paley and O’Connor, 2009). These treatments include educational and cognitive interventions, parenting interventions, and adaptive skills training. Children exposed to alcohol during pregnancy present with an array of neuropsychological deficits such as overall lower intelligence performance, impaired learning and memory and executive functioning, attention deficits, and hyperactivity. These impairments often result in educational difficulties, including inferior school performance (Mattson et al., 1998), learning disabilities (Burd et al., 2003), and classroom behavioral problems (Carmichael Olson et al., 1991). Educational interventions are focused on developing teaching strategies that facilitate learning in alcohol-exposed children, such as modifying classroom environments that may interfere with a child’s ability to learn, and providing support and resources for teachers to help them adapt their instruction and improve their ability to work with students with FASD (Paley and O’Connor, 2009). Additionally, cognitive and academic interventions aim to help enhance skills that will improve an individual’s academic performance, focusing on improving general learning skills and/or specific cognitive or academic domains (Paley and O’Connor, 2009). Some of these interventions include cognitive control therapy (CCT) (Riley et al., 2003), language and literacy training (LLT) (Adnams et al., 2007), rehearsal strategies to improve working memory (Loomes et al., 2008), and socio-cognitive habilitation programs to improve behavioral and math functioning (Kable, Coles, and Taddeo, 2007).

As mentioned above, raising children with FASD can be particularly challenging, since many parenting strategies that may be effective with typically developing children may not be successful with alcohol-exposed children. Parent-focused interventions should develop effective parenting skills, improve the parent–child relationship, decrease parent stress, and increase parental self-efficacy (Paley and O’Connor, 2009). Parent–child interaction therapy (PCIT) (Eyberg and Boggs, 1998), parenting support and management (PSM), and supportive behavioral consultation—particularly families moving forward (FMF) (Bertrand, 2009)—are evidence-based practices that provide parents with the necessary support and skills to manage the difficulties of raising a child with the consequences of PAE, and to improve their relationship with their child. Finally, adaptive skills training helps individuals with FASD to develop important age-appropriate skills that help them become less dependent on others and function more independently in their
everyday lives. Adaptive skills training may target a range of functional domains, including communication, social interactions (O’Connor et al., 2006), and safety skills (Coles et al., 2007). Clearly, a multi-faceted approach to the prevention and treatment of FAS/FASD, targeting at-risk and affected individuals as well as their families/caregivers, is important in order to mitigate the detrimental personal and societal effects of PAE.

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References


References


