

# Prenatal Drug Exposure: Behavioral Functioning in Late Childhood and Adolescence

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Following widespread publicity about cocaine babies (Kantrowitz 1990; Toufexis 1991), the American public has shown considerable concern about the potential long-term consequences to children's development from prenatal exposure to drugs of abuse. Many communities have gone so far as to consider or implement special school-based programs for children with histories of prenatal drug exposure. Yet very little is known about long-term development in children of drug-using parents and even less about what specific aspects of development, if any, are linked to prenatal exposure. Longitudinal followup of children with documented histories of prenatal drug exposure requires tremendous commitment from investigators and funders (Hans 1991), and few research studies have followed children past infancy and early childhood.

This chapter reviews the current state of research knowledge about the long-term development of children prenatally exposed to drugs of abuse. Because so little is yet known about this topic, the author discusses some general themes in the study of human development that need to be integrated into future research on older drug-exposed children.

## **REVIEW OF LITERATURE ON PRENATALLY EXPOSED CHILDREN IN LATE CHILDHOOD AND ADOLESCENCE**

Most of what is known about the late childhood and adolescent offspring of drug-using parents comes from several older studies with cross-sectional research designs. The largest such study is the work of Sowder and Burt (1980) with children of heroin addicts. Through east coast drug treatment programs, the investigators recruited a sample of children and adolescents whose mothers or fathers were former or current heroin addicts. Altogether, the sample included 126 offspring of heroin addicts between the ages of 8 and 17 years. Two-thirds of the group were African American, while the remaining subjects were of varying ethnicity. The investigators also recruited a comparison group of children from the same neighborhoods whose parents had no history of heroin use or abuse. This was done through contacting families

randomly selected from telephone directories and inquiring if the household had a child in the appropriate age range. Data for both index and comparison groups were collected from a variety of sources including interviews with the parents, interviews with the young people, school reports, and reports from a variety of community social service and law enforcement agencies.

The investigators compared children of drug-addicted and nondrug-using parents on dozens of variables, and concluded that the offspring of heroin addicts were at greater risk for a variety of problems. The index children were more likely to have missed school for reasons other than illness, and index families were more likely to have been contacted by their children's schools for absences. Eighty-five percent of index children had missed six or more days of school during the previous year, compared with 55 percent of comparison children. Teachers were more likely to have reported that index children were disobedient, did not work well in groups, were destructive of school property, and repeated grades. Index children were more likely to report having received counseling for fighting and receiving tutoring or special education. Eighteen percent of children in both groups reported having been in trouble with police, but children in the index group had a greater number of contacts with the police and more serious offenses.

Sowder and Burt did ask parents about whether the children had been exposed to drugs in utero—asking separately about heroin and other drugs, although not about alcohol. Parents reported that 44 percent of the children had been prenatally drug exposed. Comparing exposed and unexposed children on a set of outcome variable factors, the investigators found little relationship between prenatal exposure and outcome. Altogether, the Sowder and Burt data suggest that children and adolescents with drug-addicted parents are young people at risk. However, their retrospective and probably unreliable (Day and Robles 1989) measures of prenatal exposure provided no support for the hypothesis that such risk is related to the teratological effects of heroin.

That nonteratological factors might be major contributors to the behavior problems of children with drug-using parents is made even more plausible by other reports. Herjanic and colleagues (1979) studied 32 school-age and adolescent children whose fathers, but not mothers, were opiate addicts. These children, who were raised in a home with a heroin user but who were not prenatally exposed to a drug, showed outcomes very similar to those of the Sowder and Burt study, including both academic problems and antisocial behavior. Problems were more pronounced in the adolescents than the school-age children.

Wilson (1989) was the first to report a long-term followup of a sample of children with documented prenatal drug-exposure histories. Wilson conducted a partial followup of an earlier Houston sample of infants who had been prenatally exposed to opiates. This sample included fairly equal representations of African-American, Hispanic, and English-speaking white children. The followup study was conducted with limited resources, and the sample included only those families who could be reached by mail or telephone at previously identified residences. The followup sample included 68 percent of the original heroin-exposed children, 36 percent of the methadone-exposed children, and 36 percent of the unexposed control children. The total sample contained 32 prenatally exposed children and 12 controls between the ages of 6 and 11 years. Parent interviews and school reports formed the basis of the data. Wilson found a high prevalence of academic problems in both groups; one-quarter of the drug-exposed and control groups had repeated one or more grades and had required special educational services. Maternal opiate use was related to behavioral problems: 75 percent of the index cases and only 50 percent of the comparison cases were identified by parents or school as having behavior problems. Psychiatric referrals had been made for 7 index children (22 percent) and only 1 control child (8 percent).

The author recently completed a 10-year followup of a longitudinal sample of methadone-exposed children and a comparison group of unexposed children identified prenatally (for reports on this sample during infancy, see Hans 1989; Jeremy and Hans 1985). All children were African Americans living in very low income families. Over 90 percent of the original methadone-exposed sample were found and assessed (excluding children who died during the first year of life), as well as over 75 percent of the original comparison sample. Altogether, this school-age sample included 36 drug-exposed children and a slightly larger number of comparison children.

Extensive information on children's behavior problems was collected using multiple instruments and multiple informants. The parents completed the Achenbach Child Behavior Checklist (Achenbach 1991*a*), and teachers completed the Achenbach Teacher Report Form (Achenbach 1991*b*). On this instrument, teachers rated approximately half the children in both groups as having "poor" academic performance. Nationally, teachers use the "poor" rating for only 7 percent of children. The groups were also comparable in terms of the rates of retention in grade and placement in special education. Based on data from the Teacher Report Form, there was a trend for the drug-exposed children to have more externalizing problems; fully half of the drug-exposed children had externalizing scores more than one standard deviation above scale norms, although their scores were not statistically different from

those of comparison children. There were no parent-reported differences on any of the major Achenbach subscales.

The author administered a semistructured psychiatric interview that involved reports from children and their caregivers—the Diagnostic Interview for Children and Adolescents (DICA) (Welner et al. 1987). Guidelines in the "Diagnostic and Statistical Manual of Mental Disorders," 3d. ed. rev. (DSM-III-R) (American Psychiatric Association 1987) were used for diagnoses of the children based on DICA interviews data supplemented by information from the Achenbach checklists. These diagnoses were made by a psychiatric social worker who was blind to information about parents' history of drug abuse. High proportions of the children from both groups met the criteria for at least one diagnosis: 47 percent of the drug-exposed children and 37 percent of the comparison group. Diagnoses of the drug-exposed children included (in order of prevalence): attention deficit-hyperactivity disorder (ADHD), disruptive disorders (conduct and oppositional), functional enuresis, disorders of the affective spectrum, and separation anxiety. Compared with the control group, drug-exposed children were somewhat more likely to receive ADHD and disruptive behavior diagnoses but were not at higher risk for affective disorders.

Altogether these new data replicate other cross-sectional and longitudinal reports by indicating a trend for more conduct and attentional problems in children with drug-using parents. A high incidence of academic problems was observed in these children, but as in Wilson's prospective study, no differences were found between prenatally exposed and comparison children.

Ratings of symptoms are not ideal outcome measures for exploring the potential effects of prenatal exposure on child development. Behavior problems are complex and multiply determined patterns of behaviors. To detect prenatal exposure effects, one needs to look at simpler, more basic behaviors—preferably those with known links to brain damage. The author's longitudinal study included a set of neurobehavioral measures in the assessment battery. These measures included a continuous performance test (CPT) (Rosvold et al. 1956)—a computer-administered measure of sustained attention. In this task children are required to watch numbers flash tachistoscopically on a computer screen for prolonged periods, pushing a button whenever a target number appears. Outcome indices for this test have a known relationship with anoxic events at birth, even in samples of children from low-risk environments (O'Dougherty et al. 1984).

On the CPT, opiate-exposed children in the author's sample had significantly lower hit rates and higher false alarm rates than unexposed children. Low hit rates reflect deficits in basic attentional processes, while high false alarm rates reflect impulsivity. Although all children performing poorly on the CPT also received ratings of poor attention from their teachers, many other children received such teacher ratings. The CPT task seemed to be more specific to exposure history than clinical ratings of attentional problems. Further analyses are being conducted to determine whether opiate effects on attention might be mediated by environmental variables, history of perinatal problems, parental neuropsychological deficits, or other types of child behavior problems.

To summarize the knowledge of the effects of prenatal drug exposure during late childhood and adolescence, it seems that prenatally drug-exposed children are definitely at high risk for behavioral and academic problems, although possibly not any more so than sociodemographically matched controls. Since behavioral and academic problems are present even in children with drug-using parents who were not prenatally exposed, it seems unlikely that the primary source of these problems is directly related to the prenatal exposure. Nevertheless, early evidence suggests that there could be information-processing deficits observable at school age in some prenatally exposed children that might contribute to difficulties in school.

As researchers work to expand this base of knowledge on the associations between prenatal drug exposure and behavior in later childhood and adolescence, they face enormous methodological and technical challenges. These challenges are related to two of the major conceptual themes that have occupied all thinkers about human development: the nature of change and continuity across the lifespan, and the interplay between biology and experience (Kagan 1984; Lerner 1986). The remainder of this chapter elaborates on how these themes are played out in research on the long-term development of children prenatally exposed to drugs of abuse.

## CHANGE AND CONTINUITY ACROSS THE LIFESPAN

Most work in human behavioral teratology has focused on behavior during the first months after birth. This age period is the most convenient from a logistical point of view; furthermore, scientists feel more comfortable interpreting connections between prenatal events and later behavior as having a causal basis when less time has elapsed. Yet present knowledge of early problems or the lack thereof in prenatally exposed children is insufficient to permit informed statements relevant to older children. Scientists studying potential behavioral teratogens are forced to face the fact that individuals grow and develop throughout the lifespan. Different competencies are demanded of individuals at different ages. Individuals are placed in new social environments at different ages, behavior and thought are organized in qualitatively different patterns at different ages, and one would expect the effects of a teratogen to be different at different ages. The brain with its tremendous plasticity can show remarkable recovery from early insults, but new problems can emerge with development, and old problems can take different forms throughout the lifespan.

As an example of how behavioral disorders can change over the lifespan, consider the literature on individuals with ADHD. Research in behavioral teratology suggests this syndrome may be relatively more common in children prenatally exposed to drugs (Hans 1992). ADHD often goes undetected during infancy, may be first noticed during early childhood, but is most readily identified during the school years. Classic ADHD symptoms are inappropriate degrees of inattention, impulsivity, and early activity. Yet the symptoms of this disorder may change as children enter adolescence and adulthood. While inattention, impulsivity, and restlessness are likely to continue, in many cases the most salient problems of ADHD children as adolescents become antisocial behavior—defiance, aggression, temper outbursts—and sometimes substance abuse (Barkley et al. 1991; Mannuzza et al. 1991). It is assumed that much of the change in symptom expression is related to the increasing ability of individuals to control their own environment—to remove themselves from situations such as class-rooms in which prolonged quiet attention are required—and to the increasing self-awareness some ADHD children may develop at adolescence of the ways they differ from other individuals and may be limited by their behavioral characteristics.

Closer to the issue of prenatal drug exposure is recent work on the development over time of children with fetal alcohol syndrome (FAS) (Streissguth et al. 1991). These researchers reported that the predominant physical and behavioral symptoms of FAS may change at puberty. After puberty, the faces

of patients with FAS or fetal alcohol effects (FAE) are not as distinctive. Patients remain short and microcephalic, although their weight becomes somewhat closer to average. Streissguth also suggests that FAS patients have increasing behavior problems with age. Young FAS children, although intellectually handicapped, are often extremely good natured. In adolescence, attention and judgment problems remain serious, but conduct problems (e.g., lying and defiance) that had not been present at younger ages begin to emerge. Streissguth suggests that it is impossible to determine the primary origins of the behavioral problems: they could be direct results of poor environments, reflect a potentially greater vulnerability of biologically impaired children to such poor environments, or they could be the result of difficult-to-rear children eliciting nonoptimal responses from their caretakers.

Not only is it important to understand that a teratogen might alter behavior in a different manner at different ages, it is important to understand that behavioral problems can emerge at older ages that were undetectable during infancy and early childhood. The opiate drugs studied by the author for over a decade are an example of a category of drugs that appear from the literature to have little effect on child development after neonatal withdrawal. Several studies have shown small or no differences between the behavior of exposed and unexposed infants and preschool children (Hans 1992; Kaltenbach, this volume). The author's own findings of attention deficits in 10-year-old opiate-exposed children provide evidence of how effects can be discovered at a later age in a sample of children whose early development appeared normal when assessed on standardized tests. Fried's work on prenatal exposure to marijuana (this volume) is a further example of a study in which prenatal exposure effects during infancy were minimal, but became increasingly clear with age.

It is not unheard of for behavioral abnormalities whose roots may be present early in life to be undetected until later in human development. So-called sleeper effects are implicit in a number of types of brain-based developmental disorders. For example, schizophrenia is a disorder whose symptoms often emerge suddenly and dramatically in adolescence or adulthood. Yet schizophrenia is now generally believed to be a neuro-developmental disorder involving abnormalities in brain development that are present early in life, but that are not reflected in symptoms of psychopathology until much later (Fish et al. 1992; Marcus et al. 1993). Dyslexia is another disorder that cannot be identified early in life—it is not detected until children learn to read—yet it is believed to have roots in early brain development (Duane and Gray 1991; Galaburda 1993).

What are the reasons that behavioral disorders whose roots can be traced back to genetics or prenatal events are only first observable at later ages? Are there any reasons one might expect to see drug-related findings only at later ages?

Late-to-emerge effects might involve normally late-maturing competencies or aspects of behavior linked to late-maturing parts of the brain. Considerable neurocognitive development occurs during human adolescence (Flavell 1985). Human thought processes increase dramatically in complexity and abstractness, and the capacity for metacognitive processing (i.e., the capacity to think about one's own thought processes and to use that awareness to enhance thought), emerges. These changes, although not well documented, certainly involve underlying changes in brain organization. The example of schizophrenia may be relevant here also. One explanation for the emergence of the disorder later in life is that abnormalities in the prefrontal cortex are core to schizophrenia (Weinberger et al. 1991). The prefrontal cortex, involved in the highest order cognitive processes, is very late to develop pathways to other parts of the brain (Spree et al. 1984). Thus a late-to-emerge disorder such as schizophrenia may involve late-to-mature regions of the brain. Similarly, prenatal substance exposure effects that impact normally late maturing parts of the brain might not be observable early in life. Fried (this volume) argues that deficits in executive functions related to prefrontal lobe maturation similarly might not be observable in drug-exposed children until relatively late in development.

Late-to-emerge effects might also involve behavior whose emergence is triggered by hormonal changes at puberty. The most obvious example of this would be sexual behavior. Numerous animal studies suggest alterations in sexual behavior related to exposure to drugs and alcohol (McGivern, this volume; Segarra and McEwen 1992). Additionally, two studies of methadone-exposed children (Sandberg et al. 1990; Ward et al. 1989) suggest alterations in normal sexual identity related to drug exposure, particularly in male children.

Late-to-emerge effects might also involve vulnerabilities that cannot be observed until the child enters the social milieu of adolescence. Perhaps the strongest candidate for such effects would be drug-use behavior. Spear (this volume) reports animal studies suggesting that prenatal exposure may alter the adult animal's sensitivity to the effects of a drug. While it is possible that prenatal substance exposure creates a biological vulnerability to addiction in humans, such a vulnerability would normally be impossible to detect until the child matures to an age when the social environment provides opportunities for the use of drugs. Such opportunities rarely occur until adolescence or sometimes even adulthood.



To date, the published literature on the familial transmission of substance abuse has been impressively blind to the possibility that prenatal exposure might alter vulnerability to later drug use. Family studies investigating the origins of drug abuse are not as common as those studying familial patterns of alcoholism. Those that exist, such as the work of Rounsaville and colleagues (1991) with opiate addicts, have suggested that, compared with relatives of normal subjects, the relatives of opiate addicts have considerably higher rates of substance abuse. Cadoret and colleagues (1986) conducted the only adoption research focusing specifically on transmission of drug abuse. They found that substance abuse (primarily alcohol abuse) by biological parents was associated with drug abuse in offspring. These family studies, however, have not investigated the role of prenatal exposure in familial transmission.

Numerous studies of drug use in adolescents—studies sampling general populations of teenagers and studies sampling high-risk youth—have suggested that young people who initiate drug use in high school are more likely to have substance-abusing parents. With a few exceptions, the issue of prenatal exposure to substances has largely been overlooked in these studies as well. For example, Brook and colleagues (1989), who have produced much interesting information on the antecedents of adolescent drug involvement, examined the role of prenatal and perinatal factors in subsequent drug use, but failed to separate out the potential effects of prenatal substance exposure other than exposure to prescribed medications. Others (Gilchrist et al. 1990; Lohr et al. 1992) studying the drug-use patterns of pregnant adolescents examined the impact mothers' drug use had on the drug use of the adolescent, but did not try to take into account whether mothers of pregnant adolescents had been using drugs when they themselves were pregnant.

The only published human studies relevant to the issue of whether prenatal exposure creates a vulnerability to addiction in later life do not concern maternal drug abuse, but rather use of analgesic drugs during labor and delivery. In their research, Swedish investigators (Jacobson et al. 1988, 1990) recruited a sample of several hundred drug-addicted adults and their nonaddicted siblings. These individuals were identified through drug treatment programs, criminal records, and autopsy records. The researchers used the extensive Scandinavian medical databases to retrieve hospital records from the time of the subjects' births. After controlling for a variety of potentially confounding variables, they found a dose-response relationship between nitrous oxide administered during labor and the offspring's later amphetamine addiction. They also found a dose-response relationship between morphine administered during labor and later opiate addiction in offspring. These

investigators argue that these effects may be related to some kind of pharmacological imprinting mechanism involving a specific drug, but acknowledge that other factors such as prolonged perinatal hypoxia could also be involved. These study data are provocative, but remain to be replicated.

A final issue regarding change and continuity across the lifespan is understanding the stability or lack thereof of the behavior of individuals across different developmental periods. In the field of human behavioral teratology, it is also important not only to document the correlates of prenatal substance exposure at a variety of different ages across the lifespan, but also to take advantage of the strengths of the longitudinal method to document whether the same individuals are experiencing problems at different ages. Future research could pose questions such as whether the infants who have difficulties with state regulation are the same children who have attention difficulties at school age and conduct problems as adolescents. It is actually quite remarkable that, given the large number of ongoing longitudinal studies of drug-exposed children, virtually none has taken advantage of the longitudinal design to analyze patterns of behavior continuity or discontinuity over time (an exception is the work of Johnson et al. 1987).

## BIOLOGY AND EXPERIENCE

Part of researchers' discomfort with long-term followup of prenatally exposed children lies with the legitimate concern that the effects of environment on child development are important and become increasingly greater over time.

In the study of prenatally exposed children, researchers have historically gone through transformations in attitudes toward children's environments. The earliest studies of drug-exposed children tried to easily dispense with the issue of environment. They sampled unexposed comparison children of comparable socioeconomic background to the drug-exposed children and then gave no further attention to the issue of environment. As researchers became more sophisticated, they measured environmental factors and looked for exposure effects that remained significant after statistically controlling for environmental variables confounded with exposure.

Perhaps the field is on the verge of another transition: no longer viewing the environment as a nuisance variable to be ignored or controlled for. It is time that studies of prenatal exposure began to examine issues such as under what environmental conditions exposure variables are related to behavioral problems. Vorhees (1986), in stating principles of behavioral teratology,

identified this as the principle of environmental determination: "The type and magnitude of a behavioral teratogenic effect depend on the environmental influences on the organism, including both prenatal and postnatal environmental factors" (Vorhees 1986, p. 36).

At present, researchers know little about how this principle operates within human populations. Some have argued that exposure to substances can only be correlated with behavior in samples of children drawn from relatively low-risk environments; the baseline rate of problems in children from high-risk environments is simply so high that it obscures exposure effects. Fried's work (this volume) in middle-class children with prenatal marijuana exposure may be an example of how effects are more clearly identified in samples drawn from relatively low-risk environments. An opposite argument has also been made that drug exposure effects will be most clearly observable in high-risk environments. Spear (this volume) has suggested that drug exposure effects might act by creating a vulnerability to stress in offspring and therefore be particularly apparent in high-stress situations. In work on opiate-exposed children (Hans 1989), the author observed that the relationship between prenatal exposure and neurobehavioral outcome at age 2 was strongest within children from the most disadvantaged circumstances. Investigators working with human populations need to explore the moderating effects of different environmental conditions, particularly stressful conditions or potentially ameliorating conditions such as intervention and foster care. This approach requires as much care be taken with measures of environment as with measures of exposure and behavior.

A closely related research design strategy that embraces the role of environment in development explores sources of variability within groups of drug-exposed children that are related to environmental experiences. While this approach does not address basic teratology research questions, studies of individual differences within drug-exposed children may provide the most useful types of information from a clinical viewpoint. Researchers need to answer questions such as, "Under what environmental conditions do early effects of drugs disappear?" "Under what conditions do they develop into serious disorders?" "Are there conditions that foster the development of resilient children?" "Can some of these conditions be modified through intervention?" Answering such questions requires intensive longitudinal study of children's behavior and their experiences.

Although it is important to understand the basic scientific questions of whether and how prenatal drug exposure affects children's behavior, it is also important not to forget that researchers' work can answer questions that are important to

clinicians, program planners, and policymakers. Within these audiences, it is critically important to understand which children exposed to drugs in utero "make it" and which do not. Since many of the markers of "making it" or "not making it" most valued by society are only measurable at adolescence—school dropout, early parenthood, criminal behavior, drug abuse—it is obviously important to follow children until the age when these important markers can be assessed.

## SUMMARY

The knowledge base on the long-term implications of prenatal drug exposure in human development is extremely limited, but suggests that children with drug-using parents are at high risk for nonoptimal development. The literature, however, provides some evidence that this risk is related to environmental factors. To date, there is no compelling evidence that history of prenatal drug exposure affects long-term development either directly or through transactions with experiential factors.

This chapter has discussed how study of the long-term development of drug-exposed children requires careful conceptualization of issues of change and continuity in development as well as the role of biology and experience in development. Consideration of these issues will lead to fuller scientific understanding of development and also help the scientific literature better address questions of relevance to clinicians, program planners, and policymakers who are concerned with the welfare of drug-exposed children.

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