Chapter 3

THE EFFECTS OF PRENATAL COCAINE EXPOSURE

A. INTRODUCTION

Chapter 3 of the 1995 Commission Report reviewed the research on the effects of prenatal cocaine exposure on children. This section updates the 1995 report by reviewing more recent literature and research. To provide a broader context in which to assess the effects of prenatal cocaine exposure, this section also reviews briefly the research on exposure to other substances. Important findings described below include:

- The negative effects of prenatal exposure to crack cocaine are identical to the effects of prenatal exposure to powder cocaine.
- The negative effects of prenatal cocaine exposure are significantly less severe than previously believed.
- Attributing negative effects to prenatal cocaine exposure is significantly complicated by other maternal and environmental factors.

With respect to these findings, prenatal exposure to crack cocaine and powder cocaine produces similar types and degrees of negative effects, but other maternal and environmental factors contribute significantly to these negative effects.[62] In addition, research indicates that the negative effects from prenatal exposure to cocaine, in fact, are significantly less severe than previously believed. The Acting Director of the National Institute on Drug Abuse (NIDA), Dr. Glen Hanson, reports:

> [R]esearchers have found the effects not to be as devastating as originally believed, especially for children up to six years of age, [although t]here does appear to be an association between prenatal cocaine exposure and some developmental outcomes (*e.g.* attention and emotional regulation) . . . .[63]

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[62] Written statement by Ira J. Chasnoff, M.D., President, Children's Research Triangle, to the U.S. Sentencing Commission regarding Drug Penalties (Feb. 25, 2002) at 2. "[T]he home environment is *the* critical determinant of the child's ultimate outcome. . . . The drug-exposed child most often comes from a neglectful family lifestyle filled with factors that interfere with the parents' attempts at effective child rearing and participation in the growth and development of their children. . . . Further, the social environment of many addicted women is one of chaos and instability, which has an even greater negative impact on children." (emphasis added.)

[63] Hanson*, supra* note 49, at 1.

Dr. Deborah Frank, Professor of Pediatrics at Boston University School of Medicine, concurs:

> [T]here are small but identifiable effects of prenatal cocaine/crack exposure on certain newborn outcomes. . . . There is less consistent evidence of negative long-term effects up to the age of six years, which is the oldest age for which published information is available.[64]

Frank reports further that the negative effects associated with prenatal cocaine exposure (*e.g.*, premature birth, low birth weight, deficient motor skills) do not differ from the effects of prenatal exposure to other drugs, both legal and illegal, and in fact are "very similar to those associated with prenatal tobacco exposure."[65] Frank's recent analysis concluded:

> Among children aged 6 years or younger, there is no convincing evidence that prenatal cocaine exposure is associated with developmental toxic effects that are different in severity, scope, or kind from the sequelae of multiple other risk factors. Many findings once thought to be specific effects of in utero cocaine exposure are correlated with other factors, including prenatal exposure to tobacco, marijuana, or alcohol, and the quality of the child's environment.[66]

NIDA estimates that approximately 221,000 women used an illegal drug at least once during pregnancy, representing 5.5 percent of all pregnancies. Of these, approximately 45,000 women used cocaine (about 1.1% of all pregnancies).[67]

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[64] Written statement by Deborah A. Frank, M.D., to the U. S. Sentencing Commission, regarding Drug Penalties (Feb. 25, 2002) at 1. Frank concludes that "crack baby syndrome" is a "grotesque media stereotype, not a scientific diagnosis." She states, "You may recall the initial predictions of catastrophic effects of prenatal cocaine or crack exposure on newborns – including inevitable prematurity, multiple birth defects, 'agonizing withdrawal with catlike cry,' early death and profound long term disabilities for the survivors. The actual data are quite different."

[65] *Id.*

[66] Frank et al., *Growth, Development, and Behavior in Early Childhood Following Prenatal Cocaine Exposure: A Systematic Review,* 285 JOURNAL OF AMERICAN MEDICAL ASSOCIATION 1613-1625, 1613 (March 28, 2001).

[67] Hanson, *supra* note 49, at 6.

B. DIFFICULTIES ASSOCIATED WITH DRUG RESEARCH

Assessing the effect of prenatal drug exposure typically involves identifying pregnant women who use drugs before delivery (the *study* group) and gathering information on their drug use, lifestyle, and other relevant factors. At the same time a group of women are identified to serve as a comparison (the *control* group). Ideally, the women comprising the control group are identical in *every* way to the women in the study group, except in the use of the drug of interest. Although it is impossible to find a control group that perfectly matches the study group, attempts are made to match them on as many characteristics as possible, including demographic, economic, social, and geographic factors.

Although the women in the control group do not use the drug being studied, they are not excluded for using other drugs. Cocaine users may also smoke marijuana, drink alcohol, or smoke tobacco. In cocaine research, women who use marijuana, alcohol, or tobacco could be included in the control group, but women who use cocaine (or other drugs similar to cocaine) must be excluded from the control group.

During the typical maternal hospital stay, professionals who are unaware of whether the mother is in the study group or in the control group examine the newborn. Data are collected on the infant's weight, height, head circumference, gestational age,[68] APGAR score,[69] Ponderal Index,[70] and measures of the infant's reflexes and responsiveness to the environment. Study group data are then compared to control group data.

The presence and extent of other risk factors in both the study group and the control group make it difficult to attribute an irrefutable association between prenatal cocaine exposure and negative effects. These risk factors often "travel together," masking any specific relationship between the drug of interest and negative effects.[71] In his testimony, Dr. Hanson cautioned that:

Estimating the full extent of the consequences of maternal drug abuse is difficult,

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[68] "Gestational age is the number of weeks from the last menstrual period. On average, babies are born at 40 weeks gestational age. Full term babies are considered to be 37-42 weeks gestational age." http://www.dartmouth.edu/~obgyn/mfm/PatientEd/ICN_Gest_age.html.

[69] The APGAR scoring system provides a standardized means by which birth attendants can assess the baby's condition at birth and includes an assessment of skin color, muscle tone, breathing attempts, heartbeat, and response to stimulus, such as a touch or a pin-prick. http://www.birthpsychology.com/messages/apgar/apgar.html.

[70] Ponderal Index is the ratio of the weight to the length of the infant.

[71] Vincent L. Smeriglio & Holly C. Wilcox, *Prenatal Drug Exposure and Child Outcome: Past, Present, Future* (Barry M. Lester, guest ed.), 26 CLINICS IN PERINATOLOGY 1-16, 7 (March 1999).

> and determining the specific hazard of a particular drug to the fetus and newborn is even more problematic given that most drug users use more than one substance. Factors such as the amount and number of all drugs used, inadequate prenatal care, socio-economic status, poor maternal nutrition, other health problems, and exposure to sexually transmitted diseases are just some examples of why it is difficult to determine the exact effects of prenatal drug exposure. Sorting out these confounding factors is extremely difficult, [which is] why we must be cautious in drawing causal relationships in this area, especially with a drug like cocaine.[72]

To illustrate this difficulty, Table 1 presents information from a recent cocaine study comparing pregnant cocaine users with non-users.[73] While various risk factors associated with negative effects are present in both groups, women whose cocaine use was frequent (*i.e.*, daily) were older, poorer, less likely to be married, more likely to consume other drugs, and less likely to receive adequate prenatal care, all factors which also may adversely impact the health of the newborn.[74]

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[72] Hanson, *supra* note 67; *see also*, Chasnoff, *supra* note 62.

[73] Gale A. Richardson, *Prenatal Cocaine Exposure: A Longitudinal Study of Development*, 846 ANNALS OF THE NEW YORK ACADEMY OF SCIENCES 144-152, 147 (1998).

[74] Other research has also reported differences between cocaine-using mothers and the control groups with respect to other risk factors. *See e.g.*, Robert Arendt et al., *Sensorimotor Development in Cocaine-exposed Infants*, 21 INFANT BEHAVIOR & DEVELOPMENT 627-640, Tbl 2, 633 (1998); Marylou Behnke et al., *Incidence and description of structural brain abnormalities in newborns exposed to cocaine*, 132 JOURNAL OF PEDIATRICS 291-294, 292 (Feb. 1998); Virginia Delaney-Black et al., *Teacher-Assessed Behavior of Children Prenatally Exposed to Cocaine*, 106 PEDIATRICS 782-791, Tbl 1, 787 (Oct. 2000).

Table 1
Socio-Economic and Demographic Characteristics of
Frequent and Non-Using Mothers

	Frequent Users	Non-Users
Mother's Age	27 years	24 years
Percent Married	10%	26%
Family Income (monthly)	$459	$720
Percent Adequate Prenatal Care	29%	54%
Percent using Tobacco	85%	45%
Percent using Alcohol	88%	56%
Percent using Marijuana	64%	18%
Percent using Other Illicit Drugs	15%	3%

C. EFFECTS AT BIRTH

Recent research[75] typically does not distinguish between prenatal exposure to crack cocaine and powder cocaine because of the indistinguishable pharmacologic effects once the drug is ingested.[76] The findings from the cocaine research are mixed with some studies finding an association between prenatal exposure and reduced gestational age, birth weight and length,

[75] While several older studies compared the effects of crack cocaine and powder cocaine, they often suffered from methodological problems that limited their use. The more recent research examined in this chapter typically includes women who had used either crack cocaine or powder cocaine during pregnancy but then combines them into a single cocaine exposure group, making no comparisons between the two forms of the drug.

[76] Pharmacologic effects refer to the bio-chemical effects of the drug. Frank, *supra* note 64, ("[T]here are no physiologic indicators that show to which form of the drug the newborn was exposed. The biologic thumbprints of exposure to these two substances in utero are identical."); Chasnoff, *supra* note 62, at 1 ("The physiology of [powder] cocaine and crack are the same, and the changes in the dopamine receptors in the fetal brain are the same whether the mother has used [powder] cocaine or crack").

and head circumference.[77] Other researchers,[78] however, have not found these differences in cocaine exposed infants, after controlling for other fetal risk factors.[79]

Prenatal cocaine exposure has also been associated with deficiencies in reflexes, autonomic stability, motor scores, EEG sleep patterns, and regulation of state (a precursor to alertness).[80] Recent research also has found a relationship between the quantity of drugs consumed during pregnancy and the degree of negative effects on the infant.[81]

A recent study by Fonda Davis Eyler demonstrated a relationship between shorter length and smaller head circumference and the amount of cocaine used during pregnancy.[82] After controlling for other risk factors, the study found no difference in other important measures of infant health such as gestational age, Ponderal Index, birth weight and length between infants prenatally exposed to cocaine and non-exposed controls. Although the study focused on the effects of cocaine exposure generally, these findings may be ascribed in great part to crack cocaine use because crack cocaine users comprised 75 percent of the study group.

D. LONG-TERM EFFECTS

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[77] Arendt et al., *supra* note 74, at 627-640, studying a different cohort than in the 1999 research, did not find a significant difference in birth weight or head circumference; David A. Bateman et al., *The Effects of Intrauterine Cocaine Exposure in Newborns*, 83 AMERICAN JOURNAL OF PUBLIC HEALTH 190-193 (Feb. 1993); Gale A. Richardson et al., *Growth of Infants Prenatally Exposed to Cocaine/Crack: Comparison of a Prenatal Care and a No Prenatal Care Sample*, 104 PEDIATRICS (Aug. 1999). http://www.pediatrics.org/cgi/content/full/104/2/e18/html; Robert Arendt et al., *Motor Development of Cocaine-exposed Children at Age Two Years*, 103 PEDIATRICS 86-91 (Jan. 1999).

[78] Virginia Delaney-Black et al., *Prenatal Cocaine and Neonatal Outcome: Evaluation of Dose-Response Relationship*, 98 PEDIATRICS 735 (Oct. 1996); *see also* Fonda Davis Eyler et al., *Birth Outcome From a Perspective, Matched Study of Prenatal Crack/Cocaine Use: I. Interactive and Dose Effects on Health and Growth*, 101 PEDIATRICS 229-236 (Feb. 1998); Richardson, *supra* note 73.

[79] In her written statement to the USSC, Dr. Frank noted that these deficits in birth weight, length, and head circumference are similar to those found after prenatal exposure to one pack of cigarettes per day. Frank, *supra* note 64.

[80] Richardson, *supra* note 73; *also see* Fonda Davis Eyler et al., *Birth Outcome From a Perspective, Matched Study of Prenatal Crack/Cocaine Use: II. Interactive and Dose Effects on Neurobehavioral Assessment*, 101 PEDIATRICS 237 (Feb. 1998) (cocaine-exposed infants are less alert and responsive and have decreased regulation of state).

[81] The amount of cocaine used during pregnancy was inversely related to length at birth, head circumference (Eyler et al., *supra* note 78), birth weight, APGAR score, motor behavior, and regulation of state (Delaney-Black et al., *supra* note 78).

[82] Specifically, heavier average drug use during the first and third trimesters, and over the full term of the pregnancy, was correlated with length at birth, and heavier use during the second and third trimesters was correlated with smaller head circumference. (Eyler et al., *supra* note 78).

There are no published long-term studies that differentiate between prenatal exposure to crack cocaine and prenatal exposure to powder cocaine on children's development.[83] Recent research on prenatal exposure to cocaine generally indicates that the long-term negative effects of prenatal cocaine exposure do not differ from the long-term negative effects of prenatal exposure to other substances, both legal and illegal.

Studying the long-term effects of prenatal drug exposure poses additional challenges for researchers, including the difficulty of tracking often transient families for long periods of time. In addition, children exposed to drugs prenatally have an increased likelihood of living in a household of a substance abuser and being passively or directly exposed to drugs. These children also are subject to other risk factors such as poor nutrition, low socioeconomic status, and inadequate health care. The ongoing presence of these risk factors may have as great or an even greater influence than the effect of prenatal drug exposure on children's subsequent growth, performance, or behavior.[84]

To demonstrate that children prenatally exposed to cocaine are more likely to be exposed to other risk factors after birth, Table 2 compares the group of women described in Table 1 three years after giving birth. Specifically, Table 2 compares drug use three years after birth for women who were "frequent" cocaine users during pregnancy to women who were non-users during pregnancy. Women classified as "frequent" users during pregnancy used cocaine, marijuana, and tobacco at substantially greater rates three years after delivery than non-users did during pregnancy. These women also were more likely to be heavy alcohol users. Environmental factors also varied for the two groups. The homes of the "frequent" cocaine users were found to be less stimulating and less organized.[85]

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[83] Frank, *supra* note 64.

[84] Drug-exposed children often experience neglectful family lifestyles, social environments that are often chaotic and unstable, and poor family and social support systems. Poverty often exacerbates these conditions. Chasnoff, *supra* note 62.

[85] Richardson, *supra* note 73.

Table 2
Maternal Substance Use Three Years After Birth of Frequent Cocaine Users and Non-Users

	Frequent Users	Non-Users
Cocaine	28%	3%
Marijuana	24%	17%
Tobacco	76%	45%

A number of researchers have followed children prenatally exposed to cocaine for several years after birth. For children at one year of age, Richardson found no relationship between prenatal cocaine exposure and weight, length, or head circumference.[86] The study did, however, find deficiencies in motor development and temperament, including unadaptability, excessive persistence on test tasks, greater fussiness, less responsiveness, and shorter attention spans.

For children at two years of age, the Arendt study found significant differences in tests for fine and gross motor skills in the children exposed to cocaine, particularly in the areas of hand use and eye-hand coordination.[87] Recently published research of this group found significant cognitive deficits at this age in a group who were heavily exposed prenatally to cocaine.[88]

For children at three years of age, Richardson's cohort still demonstrated no differences in weight or height. However, Richardson did find smaller average head circumference, poorer performance on intelligence tests, and more behavioral problems. Examiners also rated these children as having shorter attention spans, being less focused and more restless, and more likely to attempt to distract the examiner. Richardson concluded that her study's results indicated consistent deficits in the central nervous system of children exposed to cocaine. She adds, however, that this is "the same pattern of [central nervous system] deficits [found] in our earlier studies of prenatal alcohol and marijuana use."[89]

For children at four years of age, Hallam Hurt reported no significant differences on intelligence quotient tests between children exposed to cocaine and the comparison group, after

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[86] *Id.*

[87] Arendt et al., *supra* note 77 (1999).

[88] Lynn T. Singer et al., *Cognitive and Motor Outcomes of Cocaine-Exposed Infants*, 287 JAMA 1952-1960 (April 17, 2002 reprint).

[89] Richardson, *supra* note 73, at 147, 150.

controlling for relevant confounding factors.[90] The authors noted that over 90 percent of both the study group and the control group were severely socio-economically disadvantaged and scored below average, and suggest that the effects of poverty "may have overwhelmed any effect of in utero cocaine exposure on children's [intelligence test] scores."[91]

For children four to six years of age, Chasnoff found that prenatal cocaine exposure has an indirect relationship with intelligence, but home environment is an essential intervening factor. Specifically, problems associated with prenatal cocaine exposure are mitigated in home environments rated as more adequate and exacerbated in homes rated as less adequate environments. Comparing six-year old children who were prenatally exposed to cocaine with control children whose mothers used neither alcohol nor illicit drugs, this study found that prenatal cocaine exposure was not directly related to lower intelligence scores. Living in a poorer quality environment after prenatal exposure, however, was directly related to lower intelligence scores.[92]

In contrast to the indirect relationship between prenatal cocaine exposure and intelligence scores, Chasnoff found that prenatal exposure has a direct effect on later childhood behavior problems such as managing impulses, frustration, tension, and arousal. The study notes, however, that these women were heavy cocaine users and most also used alcohol, tobacco, or marijuana. As a result, the study was unable to isolate the effects of prenatal exposure to cocaine from the effects of prenatal exposure to other substances.[93]

E. PRENATAL EXPOSURE TO OTHER SUBSTANCES

Research on the impact of prenatal exposure to other substances, both legal and illegal, generally has reported similar negative effects. For example, prenatal tobacco exposure has been associated with deficits in stature, cognitive development, educational achievement, problems in temperament, and behavioral adjustment.[94]

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[90] Hallam Hurt et al., *Children with In Utero Cocaine Exposure Do Not Differ From Control Subjects on Intelligence Testing*, 151 ARCHIVES OF PEDIATRICS & ADOLESCENT MEDICINE 1237-1241 (Dec. 1997).

[91] *Id*. at 1240.

[92] Ira J. Chasnoff et al., *Prenatal Exposure to Cocaine and Other Drugs: Outcome at Four to Six Years*, 846 ANNALS OF THE NEW YORK ACADEMY OF SCIENCES 314-328 (1998).

[93] *Id.*

[94] D. Rush & K. R. Callahan, *Exposure to Passive Cigarette Smoking and Child Development: A Critical Review*, 562 ANNALS OF THE NEW YORK ACADEMY OF SCIENCE 74-100 (1989).

Alcohol use during pregnancy has been associated with deficits in intelligence and learning problems; difficulties with organization, problem solving, and arithmetic; and lower scores on tasks involving fine and gross motor behaviors.[95] Similar to the findings presented earlier for cocaine, a dose-response relationship between the amount of alcohol consumed and the severity of negative effects has been demonstrated. In other words, using larger amounts of alcohol are associated with deficits of greater severity.[96]

Prenatal exposure to other illegal substances also has been associated with a variety of negative effects. One long-term study assessed the impact of prenatal exposure to marijuana in a low risk, white, middle class sample, and studied this group from birth until nine to twelve years of age. Use of marijuana during pregnancy was associated with increased tremors and exaggerated startle responses at birth, lower scores on verbal ability and memory tests at later ages, deficits in sustained attention in school-aged children, and behavioral problems.[97]

As with cocaine, deficiencies associated with prenatal exposure to heroin are not consistently reported.[98] Some studies find a relationship between exposure and deficiencies in motor development as well as in some cognitive measures. However, other studies that controlled for the women's use of other drugs, lifestyles, social and economic conditions, and health do not report similar findings. Regardless of control factors, newborns of women who are addicted to heroin or maintained on methadone experience a high rate of withdrawal symptoms.[99]

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[95] Ann P. Streissguth et al., *Neurobehavioral Dose-Response Effects of Prenatal Alcohol Exposure in Humans from Infancy to Adulthood*, 562 ANNALS OF THE NEW YORK ACADEMY OF SCIENCE 145-158 (1989).

[96] *Id.* These negative effects were observed at levels of alcohol abuse by pregnant women well below the thresholds associated with a diagnosis of Fetal Alcohol Syndrome or Fetal Alcohol Effects.

[97] Peter A. Fried, *Behavioral Outcomes in Preschool and School-Age Children Exposed Prenatally to Marijuana: A Review and Speculative Interpretation, in* Behavioral Studies of Drug-Exposed Offspring: Methodological Issues in Human and Animal Research (Cora Lee Wetherington et al. eds.) Series 164 NIDA RESEARCH MONOGRAPH 242-260 (1996); *see* Fried et al., *Differential Effects on Cognitive Functioning in 9- to 12-Year Olds Prenatally Exposed to Cigarettes and Marihuana*, 20 NEUROTOXICOLOGY AND TERATOLOGY 293-306 (1998). *See also* N. L. Day et al., *Effect of Prenatal Marijuana Exposure on the Cognitive Development of Offspring at Age Three*, 16 NEUROTOXICOLOGY AND TERATOLOGY 169-175 (Mar./Apr. 1994).

[98] Karol A. Kaltenbach, *Exposures to Opiates: Behavioral Outcomes in Preschool and School-Age Children,* 164 NIDA RESEARCH MONOGRAPH 230-241 (1996).

[99] Frank, *supra* note 64, at 2 indicated that prenatal cocaine exposure, unlike prenatal opioid exposure, does not cause an identifiable withdrawal syndrome in the newborn ("[A]n experienced pediatrician can walk into any nursery and identify from across the room an infant withdrawing from opiates, but an infant exposed to cocaine or crack without opiate exposure will be clinically

Finally, prenatal exposure to amphetamine and methamphetamine is associated with negative effects such as premature birth, low birth weight, small head circumference, growth reduction, and cerebral hemorrhage. At 14 years of age, children exposed to amphetamine lagged in mathematics, language, physical training, and were more likely to be retained in grade.[100]

indistinguishable from the other infants.").

[100] Mark A. Plessinger, *Prenatal Exposure to Amphetamines: Risks and Adverse Outcomes in Pregnancy*, 25 OBSTETRICS & GYNECOLOGY CLINICS OF NORTH AMERICA 119-138 (March 1998).