Specialty Conference

Effects of Transplacental Exposure to Cocaine and Methamphetamine on the Neonate

Discussant
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SUZANNE D. DIXON, MD*: Experience at the University of California, San Diego (UCSD), Medical Center with the consequences of the abuse of cocaine and methamphetamine in pregnancy is substantial and increasing. The implications for infants with in utero exposure to these drugs are becoming clearer from our own recent clinical experience and that of others. In this conference I will review what is known about antenatal exposure to these drugs and present some recent observations and experience.

Patterns of Exposure

The clinical urgency of these considerations is highlighted by the incidence of infants born at UCSD over the past four years in whom illicit drugs have been found by toxicologic assessment of the urine at birth. There was a 35% increase from 1984 to 1986 (Figure 1).

Since then there has been an almost fivefold increase in the incidence. These numbers do not include infants in whom there was exposure early in gestation or those from whom the drugs cleared before birth. Therefore, these numbers vastly underestimate the full extent of the problem. Similar increases have been reported from virtually every major urban center. For example, Los Angeles County reported a doubling every year since 1983 of the number of infants born with illicit drugs in their urine. Other centers cite the incidence of this problem at 10% to 25% of neonates. These increases in rates are accounted for largely by an increase in the use of stimulant drugs, cocaine, methamphetamine, and, to a lesser extent, hallucinogens such as phencyclidine hydrochloride.

It is estimated that 50 million Americans have tried cocaine and that 8 million use it regularly. Between 10% and 20% of the adult population uses some nonprescription, psychoactive drug regularly. By one estimate, 12% of young adults have severe addictive disease. Although the increasing use of alcohol and other drugs among adolescents is a major concern and the target of educational programs, most drug users are 20 to 35 years of age, the childbearing years. The greatest increases in drug use starting in the 1970s and accelerating in the 1980s are among young adults. The perinatal impact of this issue is a direct result of the broad increase in drug use in this segment of the population.

The pediatric community was unprepared for this epidemic in our nurseries. Reports of the effects of cocaine on adults began to emerge after 1982 and exploded onto the pages of the popular press. The effects on the fetus were largely unknown. Reports of the consequences of amphetamine exposure on the unborn were few. The only available model in pediatrics was our experience with neonates having exposure to opiates. The course of withdrawal and outcome for heroin- and methadone-exposed children has been well described, for instance, by Volpe.[1(p616)] The signs of neonatal narcotic withdrawal are quantified in scoring formats such as that developed by Finnegan.[2(p262)] Although these schemes allow us to monitor and treat neonates who have exposure to opiates and other central nervous system (CNS) depressants, this familiar approach could not readily be applied to these new stimulant drugs and their new multiorgan effects.

History of Cocaine Use

Cocaine (Figure 2) is derived from the *Erythroxylon coca* plant grown in the mountains of Latin America. The leaves of this plant have been chewed by members of Indian tribes for perhaps 5,000 years to abate hunger and improve work endurance. Cocaine was isolated and introduced to northern industrial countries in 1859. Fans of Sherlock Holmes know the role the drug played in his creator's life. Freud praised the stimulant properties of the drug despite the fact that he lost a friend and patient to a toxic overdose. Coca Cola contained the drug until 1903. By 1906 awareness of the toxic potential of cocaine led to restricted access, with its being used primarily as an anesthetic for ear, nose, and throat and ophthalmologic operations. Recreational users were few in number and usually wealthy, as the drug was expensive. A resurgence in the popularity of cocaine began in the 1970s, but the astronomic rise in its use in this country occurred in 1982, along with a dramatic increase in illegal imports. The newspaper and television reports of the deaths of prominent athletes and entertainers brought to almost every household an awareness of this drug and its toxic consequences.

A primer on cocaine is given in Table 1.

Pharmacology of Cocaine

The powerful euphoric effects of cocaine depend largely on the CNS release of dopamine, which is followed by depletion of that compound, leading to the "crash" or abstinence syndrome characteristic of this drug. Cocaine also facilitates the release of serotonin and other neurotransmitters.[3] It has

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ABBREVIATIONS USED IN TEXT

CNS = central nervous system
UCSD = University of California, San Diego

been described as a uniquely American drug that imparts a sense of power, increased self-esteem and vigor, decreased fatigue, and an increased sense of sexual prowess. Hypersomnolence, hyperphagia, irritability, and depression are the down side of the cocaine cycle. Investigators now accept cocaine as a physically addictive drug, particularly when taken in high concentrations, such as with "crack" or "rock" cocaine.[4]

In addition, cocaine blocks the presynaptic reuptake of norepinephrine and increases the amount of that substance at postsynaptic receptor sites throughout the body. Over time, there is a net depletion of norepinephrine. There is an increase in the activity of the sympathetic nervous system, a decrease in peripheral nerve conduction, and direct action on some smooth muscle groups.

The toxic effects follow from this pharmacologic action (Table 2). The most important effect of this drug is powerful vasoconstriction. Essentially every organ system is vulnerable to this vasoconstrictive action. The cardiac effects have received the most press, but multiple organ systems show the toxic effects of this drug.[4]

The plasma half-life is about 30 to 40 minutes. The drug is detoxified by cholinesterases in plasma and liver. The plasma enzyme has wide individual variation, which may account for the variable and unpredictable toxicity of cocaine. Cardiac morbidity appears to be unrelated to the dose, duration of usage, underlying disease, or route of administration. This unpredictability makes cocaine a dangerous drug; it dissolves some popular myths regarding cocaine, such as "snorting the drug is OK; smoking and inhaling it is not"; "I use it only at parties, so I'm safe"; "cocaine is not addictive; it's easier to kick than heroin." Of importance for pediatricians is that the activities of cholinesterases are at relatively low levels in pregnant women, fetuses, and newborns. As a group, perinatal patients might be predicted to be more vulnerable to the toxic effects of this drug.

Cocaine is metabolized to benzoylecgonine and ecgonine, distinct substances that can be identified by several commonly used toxicologic assessments. Immunoassay of the urine may give positive results as long as five days after use in nonpregnant adults.

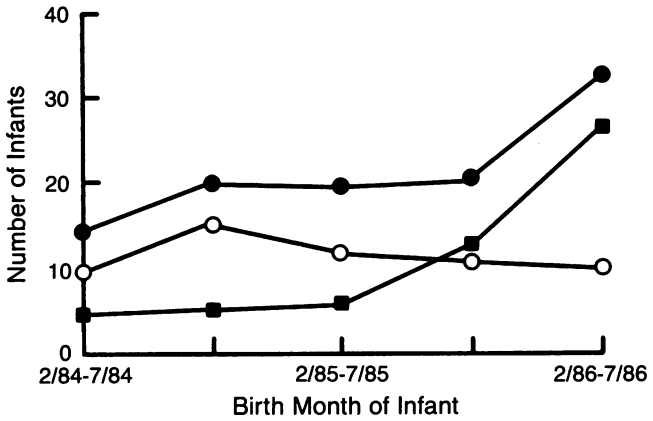

Figure 1.—Patterns of drug exposure are shown for infants born at the University of California, San Diego, Medical Center from 1984 to 1986. ● = total documented drug-exposed infants, ○ = infants with narcotics exposure, ■ = infants with stimulants exposure

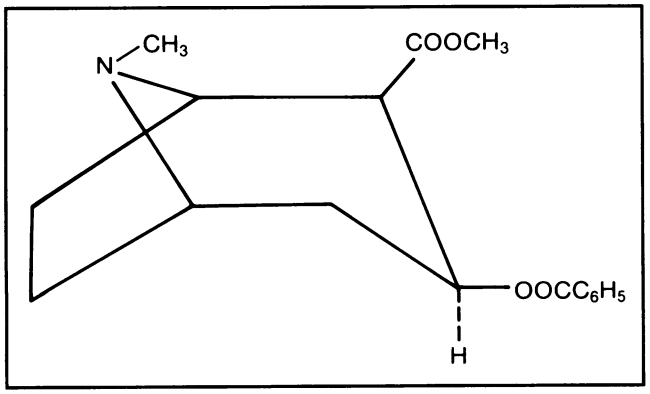

Figure 2.—The structure of cocaine is shown.

TABLE 1.—*Cocaine Primer*

Derived from leaves of *Erythroxylon coca*
Imported as a white powder, often mixed with talc, lactose, or dextroamphetamine sulfate
Simple molecule, easily absorbed across any membrane for use intranasally, intravenously, intramuscularly, subcutaneously, orally, sublingually, intravaginally, intrarectally; present in breast milk
Easily made into hydrolyzed crystal—"crack," "rock"—that is easily vaporized—"smoked"—with rapid absorption and high concentration; this form is rapidly and strongly addictive
Although cheaper by the dose, the duration of the high with "crack" is brief and the addictive potential high
Street names: "coke," "snow"; when combined with heroin, "speedball"
Often used with depressants, alcohol, or heroin
Produces euphoria, increases activity and gregariousness; reduces appetite and sleep
Metabolized to benzoylecgonine and ecgonine and detectable in urine for as long as 5 days in the average nonpregnant adult

TABLE 2.—*Clinical Consequences of Cocaine Use in Adults*

Cardiovascular
Hypertension, tachycardia
Cerebral infarction
Nonthrombotic myocardial infarction
Ventricular arrhythmias
Subarachnoid hemorrhage
Ruptured aneurysms, peripheral and central nervous system
Aortic rupture
Renal infarction
Bowel infarction
Chronic colitis
Dermatitis, presumably related to small vessel disease
Central Nervous System
Euphoria, increase in activity, and increased sense of creativity and sexual prowess
Psychosis, hallucinations
Depression
Seizures
Respiratory arrest
Labile affect, panic disorder, aggressive ideation and behavior
Decreased total sleep and selective reduction of rapid-eye-movement sleep
Other
Fever or malignant hyperthermia
Anorexia
Midriasis
Perforated nasal septum
Infectious disease risk associated with life-style issues and, in a minority, intravenous use

Complications of Cocaine Use in Pregnancy

Studies in animals carried out at UCSD and elsewhere have revealed decreases in uterine and placental perfusion and a direct increase in uterine contractility following the administration of cocaine.[5] Observations in women are consistent with these findings. There are sharp increases in fetal wastage, increases in the incidence of placental abruption, and precipitous onsets of labor following cocaine use. In one study of otherwise healthy "recreational" users of cocaine in Chicago, Chasnoff and co-workers noted a 23% spontaneous abortion rate.[6] A comparison of the histories of pregnant women using drugs indicated an incidence of spontaneous abortions among users of cocaine more than twice that of a group of users of heroin (38% versus 16%). The mean number of previous spontaneous abortions was also increased in the cocaine-using group (0.98 to 1.1 versus 0.47 to 0.9). The highest fetal wastage was among cocaine and heroin users: 46% reported a previous spontaneous abortion, and the mean number was 1.3 to 1.2 per woman. Data from our Teratogen Registry at UCSD indicate a 28% spontaneous abortion rate among women calling early in pregnancy because of concern about their self-described "recreational" cocaine use (K. L. Jones, MD, oral communication, 1987).

Increased systolic blood pressure, decreased uterine and placental perfusion, and increased uterine contractility may all contribute to the consistent observation by several investigators of about a tenfold increase in the incidence of placental abruption, hemorrhage, or both associated with cocaine use.[4-6] There are several clinical reports of the immediate onset of contractions after cocaine administration, and our own clinical interviews support this. Street lore supports the notion that cocaine use "starts the baby"—that is, starts labor.

A study in sheep suggests that cocaine administered to ewes results in more fetal distress than the direct intraamniotic administration of the drug to the fetal lamb.[7] The decreased placental perfusion and resultant anoxia in the fetus may be more detrimental than direct effects of the drug.

An interesting study from Northwestern University Medical School (Chicago) showed alterations in placental neurotransmitter receptors in tissue obtained from drug-using women. The supposition is that these alterations reflect similar chronic changes in the fetal brain. Although preliminary and based on a study of polydrug users, the findings suggest important opportunities for research aimed at assessing neurotransmitter systems in the developing brain. In that study, the most deviant values were seen in the placenta from a stimulant drug-using woman, presumably due to the direct alteration in the neurotransmitter system associated with these drugs.

Neonatal Consequences of Cocaine Use

Cocaine crosses the placental barrier by rapid simple diffusion. A variety of skeletal defects, exencephaly, hydronephrosis, and cryptorchidism, were described by Manhalik and colleagues in a mouse model of antenatal cocaine use.[9] In a clinical report from New York, skull defects were identified in a number of infants, and there was an increase in the incidence of congenital heart disease among a group of urban minority-group neonates.[10] Chasnoff and Chisum reported three instances of the prune-belly syndrome,[11] one they related to a single large maternal dose of cocaine taken at five weeks' gestation,[6] a critical time in the development of the urinary tract. They also reported a 13% incidence of obstructive uropathy in this group with mild hydronephrosis, and, of 81 infants studied prospectively with renal ultrasonography, 6 had hypertension. No child has yet been noted with any long-term alteration in renal anatomy or function. We have not seen this in more than 100 infants studied, although transient hypertension frequently occurs.

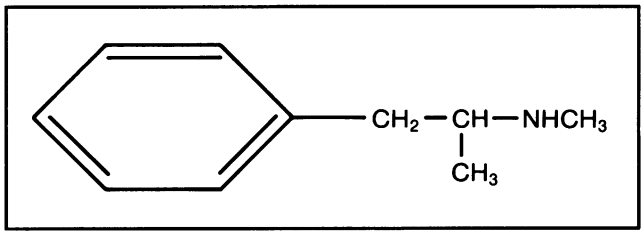

Figure 3.—The structure of methamphetamine is shown.

There is a growing consensus that cocaine produces intrauterine growth retardation and, in particular, a reduction in brain growth. In a recent report,[12] altered lymphocyte function was noted among infants born of human immunodeficiency virus-negative intravenous drug abusers, 44% of whom used cocaine and amphetamines.

Acute cerebral hemorrhagic infarction,[13] white matter cavitary lesions, and other abnormalities were identified by cranial ultrasonography in 12 (37%) of 32 cocaine-exposed neonates.[14] Two instances of myocardial infarction have been identified in cases of immediate antenatal usage. We have seen two term infants with an acute infarction of the bowel at birth, possibly related to maternal usage of cocaine.

Cocaine readily crosses into breast milk, with adverse consequences for the newborn child.[15,16]

In summary, these reports do not appear to support a concept of distinct embryopathy related to cocaine use. Multisystem abnormalities of a variety of types might be anticipated, in view of the vasoconstrictive properties of this drug, the variability depending on the dosage, the time of exposure in relation to fetal development, and individual variation.

Methamphetamine Use

The first cousin of amphetamine, methamphetamine (Figure 3), enhances the presynaptic release of norepinephrine, alters CNS neurotransmitters, and in these respects has pharmacologic effects nearly identical to those of cocaine.[3] It is excreted unchanged and as amphetamine for as long as two days after its use in adults. Immunoassays for this drug are confounded by its cross-reactivity with a variety of drugs, including cold remedies and tocolytic agents. Amphetamine use in adults results in central nervous system excitation, followed by a withdrawal period characterized by prolonged sleep, lassitude, fatigue, hyperphagia, and vivid dreams. Long-term use is associated with an aggressive paranoid psychosis and a pattern of deep-brain strokes. Vasospastic strokes, ruptured cerebral aneurysms and infarctions around the basal ganglia, and a cerebral angiitis are seen in cases of adult amphetamine use. Lead poisoning related to manufacturing techniques has also been reported as a complication of methamphetamine use in adults. A primer of methamphetamine is provided in Table 3.

Methamphetamine is the most commonly abused drug in San Diego County. It accounts for 33% to 40% of referrals to treatment centers and represents more than 60% of seizures of illicit drugs by law enforcement. Other rural or semirural

areas are also experiencing an increase in the use of this "homegrown drug."

Amphetamine Use in Pregnancy and the Neonatal Period

The methyl radical has been added only recently, and previous medical reports of illicit amphetamine use are primarily of intravenous use. In the 1950s obstetricians prescribed low oral doses of amphetamine to reduce weight gain in pregnancy; no structural abnormalities were found in those children. In 1974 Ramer described an infant with exposure to illicit amphetamine who had hypoglycemia, sweating, poor feeding, and poor visual tracking with deviations of the eyes.[17] The infant had periods of having a dusky color and had a "glassy-eyed" appearance. A clinical seizure in the absence of electroencephalographic changes was noted on day 6 of life. The child was described as normal at 2 years of age, but no detailed neuropsychological tests were reported.

The largest series of observations has come from the Karolinska Institute in Sweden.[18] Infants reportedly were born to two groups of mothers, one of which stopped the intravenous use of amphetamines during their pregnancies, while the other continued using the drug throughout. There was an increased incidence of morbidity in both groups, but problems were more severe in the group that continued to use the drug. Alcohol use was high in both groups. There was an increase in the incidence of preterm labor, placental abruption, fetal distress, and postpartum hemorrhage. Normal somatic growth was noted by one year despite an increased illness and accident rate in these groups. The infants with continued exposure were smaller and had feeding difficulty to the point of requiring gavage feedings. Drowsiness and lassitude lasted several months in these infants. Development was described as "very slow" for six months for those infants who went to foster homes and presumably received better care and observation. The foster mothers often suspected hearing loss, but none was found. Perhaps they were responding to a decreased quality of alertness in those children.

TABLE 3.—*Methamphetamine Primer*

- Produced locally in stills using simple chemicals, primarily ephedrine
- White powder that is taken intranasally (rarely by injection), with the rapid onset of a "high"
- Regularly used with large amounts of alcohol or other depressants
- Street names: "crystal," "crystalmeth," "speed"
- Chronic user: "speed freak"—usually indicates chronic psychiatric impairment
- Metabolized to amphetamine and identified in urine for 1 to 3 days in an average adult
- Cross-reacts in immunoassay with antihistamines and other cold remedies and tocolytic agents
- Has been associated with cardiovascular morbidity, acute psychosis, malignant hyperthermia, and hypertension
- Ruptured cerebral aneurysms, basilar brain infarctions, cerebral angiitis, and other intracerebral hemorrhages also occur

The San Diego Experience

In a retrospective analysis of our own experience in San Diego from 1984 to 1986,[19] we compared the perinatal courses of infants in whom cocaine or methamphetamine was present in the urine at birth. This presumably represents a population in whom there was relatively high or prolonged drug exposure, although precise drug use data are inaccurate in almost all clinical settings. Regarding maternal medical factors, we found that the two groups showed no significant differences (Table 4). Both groups consisted of women in their mid-20s, usually with other children; less than 5% were younger than 21 years. There was an increase in the incidence of placental abruption in both groups. Most of the women received no or limited prenatal care.

The neonatal outcomes were also comparable in the cocaine- and methamphetamine-using groups: intrauterine growth retardation, decreased head circumference, preterm

TABLE 4.—*Maternal and Neonatal Morbidities Associated With Cocaine and Methamphetamine Use in Contrast to a Medically and Demographically Similar Control**

	Drug Use			
Demographics	*Cocaine, n=13*	*Methamphetamine, n=28*	*Control, n=45*	P
Maternal				
Maternal age, years	26.1±4.8	24.1±4.6	25.8±5.9	NS
Gravidity	3.7±2.6	3.2±1.5	3.3±2.1	NS
Parity	1.7±1.1	1.6±1.0	2.1±1.4	NS
Abortion	2.0±1.8	1.6±2.5	1.2±1.4	NS
Prenatal care				NS
Complete, %	0	0	7	
Limited, %	69	57	64	
None, %	31	43	29	
Nicotine use, %	38	31	...	NS
Ethanol use, %	46	20	...	NS
Neonatal				
Gestational age, weeks	37.5±3.1†	38.1±3.1‡	39.4±1.4	.01
Birth weight, grams	2,719±739†	2,955±710	3,246±522	.02
Length, cm	47.6±4.9†	48.1±5.7‡	50.7±2.8	.02
OFC, cm	32.6±2.8†	33.2±2.1‡	34.3±1.5	.006
Apgar score				
1 min	7.8±0.6	7.4±2.1	8.0±2.0	NS
5 min	8.8±0.4	8.4±1.5	9.0±1.0	NS

NS=no significance, OFC=occipitofrontal circumference

*Except for percentages, values are the mean ± standard deviation.
†$P<.05$ Cocaine versus control groups.
‡$P<.05$ Methamphetamine versus control groups.

delivery with fetal distress, and anemia were common in both groups.

The withdrawal course, as monitored by the Finnegan scoring system,[2] was abnormal in similar ways; CNS symptoms predominated. Most infants had symptoms that included abnormal sleep patterns (81%), tremors (71%), hypertonia (52%), high-pitched cry (42%), poor feeding (58%), vomiting (51%), sneezing (45%), frantic sucking (42%), and tachypnea (18%) (Figure 4). Three methamphetamine-exposed infants required gavage feeding because of lethargy and poor feeding.

In comparison to a narcotic-exposed group, the combined stimulant group, including infants with exposure to both cocaine and methamphetamines, had similar reductions in intrauterine growth and less severe abstinence scores.

In comparison to an economically, racially, and sociologically comparable drug-free group, all the neonates with drug exposure had more adverse perinatal outcomes and a higher incidence of preterm delivery, lower birth weights and head circumferences for gestational ages, and a higher rate of anemia (Table 5). Indeed, when all the perinatal features, including adverse demographic and economic factors, were analyzed using a multiple regression format, only drug exposure contributed statistically significantly and adversely to intrauterine growth and gestational age in both the cocaine- and methamphetamine-exposed groups. This effect seems to be over and above the deleterious effects of poverty, poor nutrition, and a lack of prenatal care that always confound the clinical situation.

Between January 1987 and July 1988, we have seen 103 new term infants with exposure to the following drugs: cocaine, 41%; methamphetamine, 30%; opiates, 8%; and combined cocaine and heroin, 22%. During this time, essentially all of the heroin users also used cocaine, which is a new trend. This is consistent with the data from New York, where 36% of "compliant" methadone users and 80% of heroin users also used cocaine. This means that even that old familiar group, narcotic-exposed neonates, will be more challenging because of this combined exposure. In this "speedball" group, the morbidities were of the same variety, only more severe: prematurity rate, 45%; small for gestational age, 46%; and reduced occipitofrontal circumference for gestational age, 29%. Withdrawal is more prolonged and severe in this group, and the mothers are farther away from recovery.

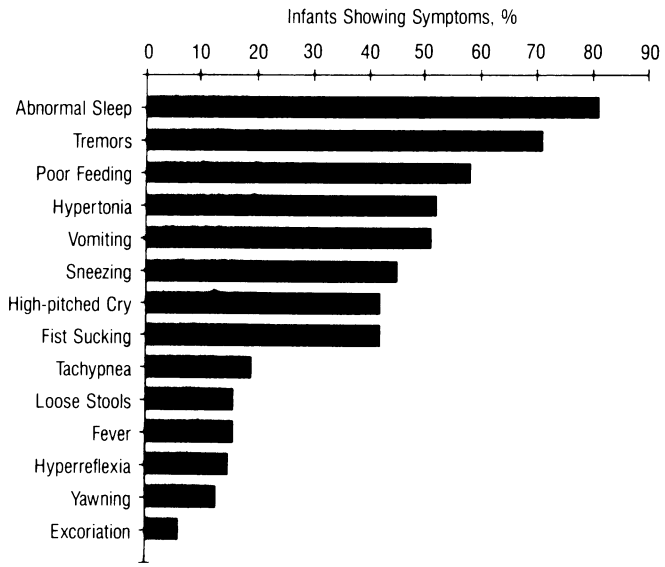

Figure 4.—The graph shows the neurobehavioral symptoms seen in neonates with exposure to stimulant drugs. Most infants showed some abnormal neurologic and physiologic behaviors suggestive of drug effect or withdrawal.

TABLE 5.—*Perinatal Morbidities of Drug-Exposed Infants, %*

Perinatal Morbidity	*Stimulants,* n=46*	*Narcotic, n=49*	*Control, n=45*
Prematurity	28†	22‡	9
Small for gestational age	9	9	2
Small head circumference for age	17	17	4
Fetal distress	39	38§	24
Bradycardia	22	24	17
Meconium	17	11	7
Placental hemorrhage	13†‖	2	2
Anemia	13†‖	2	0
Seizure	2	8	0
Cerebral infarction	2	0	0

*Cocaine and amphetamines.
†$P < .05$ Stimulant versus control groups.
‡$P < .05$ Narcotic versus control groups.
§Three infants had variable deceleration.
‖$P < .05$ Stimulant versus narcotic groups.

Demographically, the cocaine and methamphetamine users are distinct groups. The cocaine users tend to be of inner-city minority groups, initially all black but now 25% Hispanic. They are Medi-Cal recipients but rarely have sought access to care. In contrast, users of methamphetamine in San Diego are predominantly white and come from all areas of the county, including semirural areas. They have no health coverage, have high unemployment rates, and are largely outside of systems of care. These are angry, aggressive, difficult parents who have strong denial mechanisms and chaotic life-styles. The cocaine-using parents are either so locked in by drug abuse that they are unable to care for their infants or they present with management problems common to poor, inner-city minority families. The newly emerging group of Hispanic women appears to be recently recruited to the drug scene through cocaine. Heroin is used as a secondary drug to dampen the "crash" of cocaine. Although phencyclidine use is growing among Hispanic communities, we have seen little of that in our neonates. In contrast, infants with exposure to phencyclidine are common in Los Angeles County.

Our clinical observation indicates that the abstinence scoring derived from the narcotic model does not capture the full range of behavioral alterations seen in infants with exposure to stimulant drugs. A series of Brazelton Neonatal Assessment Scale examinations were initially done on 15 infants with exposure to cocaine and now on a larger sample of 60. These studies have indicated a pronounced alteration in visual processing, quality of alertness, tremulousness, and startle reflex. Abnormalities of a similar but less dramatic nature had been reported by Chasnoff and associates.[6] Children with exposure to methamphetamine showed similar but less severe alterations in newborn behavior in this examination.

The visual system appeared particularly impaired after exposure to either stimulant drug. Flash-evoked visual potentials were assessed in 17 cocaine-exposed infants[20] and were abnormal in the vast majority. In subsequent studies, 62 (78%) of 80 had abnormal visual potentials, and more than

half remained abnormal through the first year. The long-term outcome is unknown.

Several mechanisms could account for this. First, visual processing as a sophisticated system in neonates may be more sensitive to a more generalized neurophysiologic disturbance. Second, changes in retinal and conjunctival vasculature have been described in adult users and passively exposed infants. We have not seen retinal changes in the infants assessed so far, but a prospective study is clearly needed. Third, certain areas of the brain coordinating visual processing may be particularly affected, either through vasoconstrictive necrosis in, for example, the frontal lobes or through alterations in neurotransmitters. These mechanisms are speculative at this time.

Electroencephalographic changes were noted in this population[19] that consisted of an increase in positive sharp wave activity, particularly in the frontal and central vertex regions, and an increase in the wave activity. These are suggestive but not diagnostic of white matter disease. Four children were found to have seizure discharges, evident clinically only by a substantial decrease in alertness. A pronounced alteration in sleep-wake cycles was seen in the majority of children.

Following the report of neonatal stroke, we began to look at ultrasonographic examination of the brain.[14] One cocaine-exposed infant appeared to have had a similar cortical wedge lesion that occurred before birth. This was confirmed by a computed tomographic scan that also showed diffuse white matter attenuation suggestive of previous ischemic damage. A third of the 74 term infants studied, who were otherwise entirely well, have had evidence of brain hemorrhage, cavitation, or infarction commonly involving the basal ganglia around the internal capsule or deep in the frontal lobes, atrophy, or major hemorrhage in the posterior fossa. The evolution of these perinatal infarcts is shown in ultrasonographic images in Figure 5.

Computed tomographic and magnetic resonance imaging scans show diffuse cerebral atrophy or what appears to be delayed myelination. The small size of these lesions may require further refinements of imaging techniques. Areas of infarction and cystic change on cranial ultrasonograms are distinct from the hemorrhagic periventricular leukomalacia seen in preterm infants that may be the antecedent of classic spastic diplegia. These areas appear to be functionally "silent" in the newborn period as the location of these lesions is distinct.

Follow-up Studies

This population of children is extremely difficult to follow up, and there are no large long-term studies of physical and behavioral development of neonates with exposure to stimulant drugs. In our own experience, 59% have gone to foster homes initially. At the end of one year, about 30% have

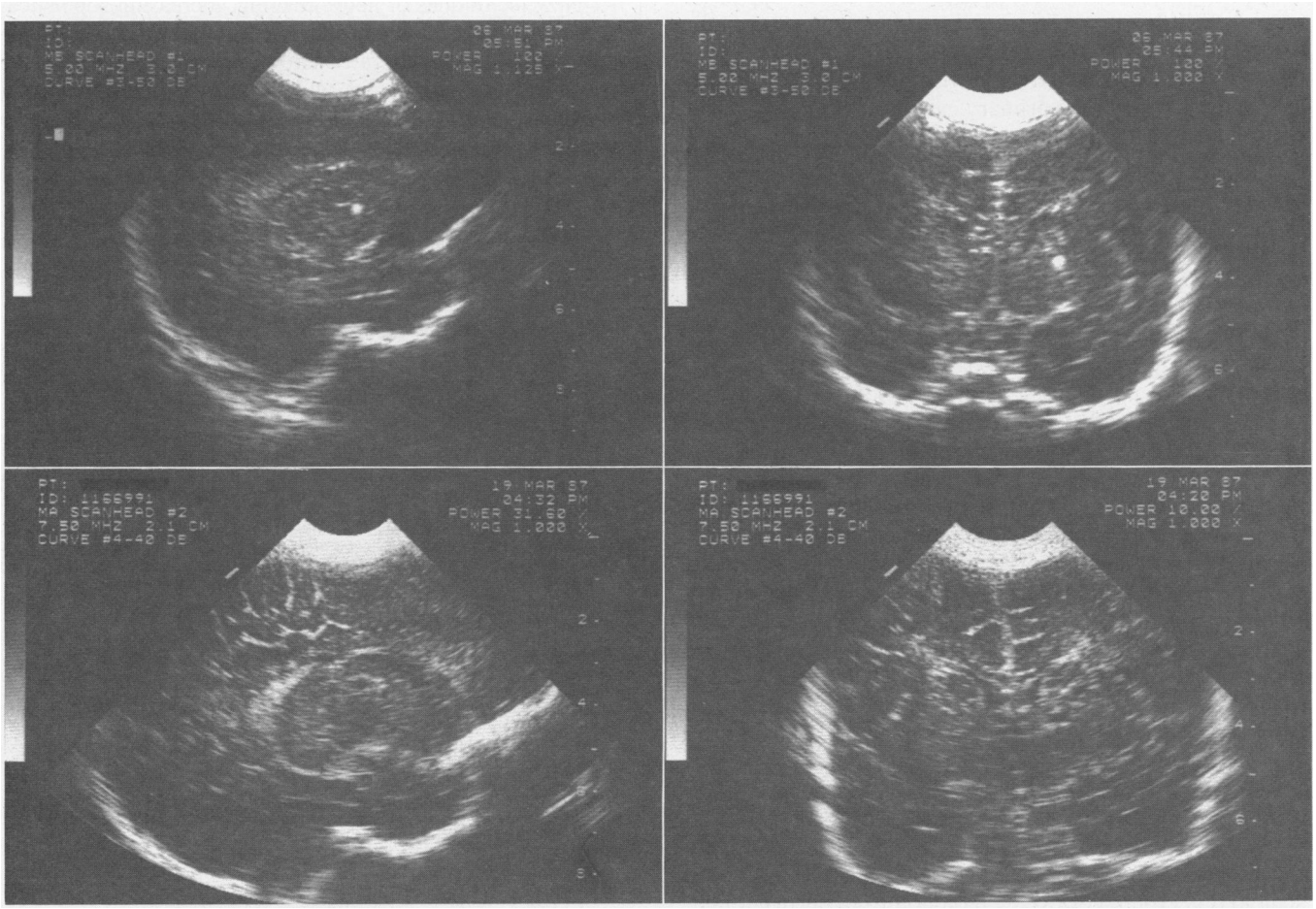

Figure 5.—Upper left, A parasagittal cranial ultrasonogram on day 1 shows an area of hemorrhage (round white lesion) at the base of the brain. **Upper right,** A coronal section taken of the same infant on day 1 of life validates the area of acute hemorrhage inferior and lateral to the lateral ventricles. **Lower left,** A parasagittal study on day 14 of life shows that the hemorrhagic area seen in the initial study has now become cystic (dark) and other echolucent areas are seen around it. **Lower right,** The coronal view also shows the cystic infarctions on day 14 where hemorrhage was seen earlier.

remained in foster care, but two to three shifts of homes is common. For infants who go home with their mothers, chaotic life-styles continue, even if drug use by the parents is eliminated. Recidivism for treated chemically dependent parents remains high.

Developmental assessments of our population have shown that about three fourths have developmental quotients of less than 100 during the first year, with areas of fine motor and visual motor coordination showing the greatest delays. In these areas there is a decrement of performance related to age in a cross-sectional group of these children. Fine motor development appears more compromised as the children mature, compounded by the fact that more fine motor items are assessed at older ages. This observation is consistent with our clinical impression that visual-motor coordination is selectively impaired in both cocaine- and methamphetamine-exposed neonates. More formal analysis is in progress. As a group, however, these children certainly warrant close developmental assessment, particularly as the structural brain lesions are concentrated in areas that may not show impaired function until school age.

Infants with exposure to cocaine apparently go through a secondary withdrawal phase of neurobehavioral disturbance at 2 to 8 weeks of age. They are extremely irritable, hypertonic, sweaty, mildly febrile (38°C [100.2°F]), hyperphagic, and have notable decreases in sleep. Typically the weight not only catches up but becomes excessive. The usual supportive measures, including pacifiers and rocking, that are used for narcotic-exposed infants appear ineffective. About 25% of these children have been treated with phenobarbital, regardless of the source of the primary care prescriber, and it was reported that sleeping and eating patterns improved.

Foster parents have described these infants in vivid terms: "He shakes all the time, even when he sleeps." "He just sweats; he goes hard at things." "She hates the world; she's so angry." "I can't stop him from eating—nothing else works." "He keeps the house up all night." "Holding her doesn't seem to help." "This is the worst drug kid I've had."

In this group, we have seen children with spastic quadriparesis, hemiplegia, microcephaly, global delay, and seizures. We have also seen an 8-month-old infant whose hyperactivity was to such a degree that the administration of methylphenidate was suggested by two other providers. A turbulent neonatal course appears to be associated with a more severe subacute withdrawal phase. It is in this group that the most severe neurologic impairments occur.

In contrast, methamphetamine-exposed infants as a group appear less impaired in the first year. They exhibit lethargy, poor feeding, poor alertness, and severe lassitude. They are described as follows: "Her eyes are glassy." "He forgets to suck while I'm feeding him." "He stares up at his mobile, but I don't think he follows it." "She's such a good baby—she never cries." "She's very quiet." "Her eyes are blank." Most of these children have minor neurologic abnormalities, but development is usually within normal limits during the first year. Three infants have been readmitted with medical problems compounded by severe neglect. Some of the most severe, unusual, and surprising outcomes have been seen in this group, however. Prediction from perinatal findings is poor. Oculomotor apraxia, a parkinsonian dystonia, a severe tactile-elicited dystonia, pronounced intention tremor, severe active hypotonia, and a hemiparesis developed in children in this group after a relatively benign neonatal course. Many of the abnormalities suggest frontal lobe dysfunction that may only be manifested at school age. Severe visual motor difficulties were noted in two otherwise normal preschoolers who were known to have had antenatal exposure to methamphetamine.

Conclusion

Neonates who have had exposure to cocaine or methamphetamines are with us in ever-increasing numbers. They challenge every child care provider in health, education, and in the social and legal systems. The hold of chemical dependency on parents makes it difficult for them to meet the needs of these children without an expansion of existing treatment facilities. The foster care system is vastly overburdened. We have reason for very major concerns about the outcome of this population. In contrast to heroin and methadone—which are detrimental to children also—these drugs have the potential for serious structural damage to the central nervous system that has implications for long- and short-term development. Although many infants present challenges in the first year of life, others may emerge only at school age with handicaps that impinge on their development. By comparison, this epidemic will make the one of neonatal narcotic exposure seem a simpler and less disabling disorder.

New techniques of neuroimaging, increasing sophistication in neurobehavioral assessment, and advances in neurochemistry can be integrated into new understandings of the structural and functional relationships in the developing brain in this clinical population, as we attempt to cope with and eradicate this horrible human experiment.

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