

eNeonatal Review

Jointly Presented by The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing

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In this issue...

Methamphetamine, a highly-addictive stimulant, was first synthesized in 1893 by a Japanese pharmacologist and its addictive potential became evident after World War II. While it has been abused in pockets of the United States for decades, currently its growing use throughout the country is attracting the attention of the medical and law enforcement communities as well as the media. Physiologically, methamphetamine appears similar to cocaine, but it is less expensive and far longer acting, suggesting great potential to supplant cocaine as the drug of choice in many areas.

For the neonatologist, knowledge regarding the effects of methamphetamine is important because women of childbearing age appear to have high rates of abuse and adverse neonatal effects have been described. Methamphetamine-exposed infants are frequently premature and born to mothers with little prenatal care. Other comorbid medical and social conditions exist that mandate a team approach involving obstetrics, neonatology/pediatrics, social work, and state social services.

In this issue, we review existing animal and human studies that describe fetal methamphetamine physiology and the effects of antenatal exposure on neonatal growth, brain structure and neurodevelopment, and discuss research reporting the child abuse and neglect potential among methamphetamine users.

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Learning Objectives

The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing take responsibility for the content, quality, and scientific integrity of this CME/CE activity.

At the conclusion of this activity, participants should be able to:

- Describe the association between prenatal methamphetamine exposure and decreased fetal growth;
- Discuss the central nervous system damage, including intraventricular hemorrhage, white matter lesions, and decreased growth of subcortical gray structures, associated with fetal methamphetamine exposure;
- Identify the neurobehavioral alterations in the newborn produced by antenatal methamphetamine exposure.

Recommend to a Colleague



Commentary

The use of methamphetamine (also known as “meth”, “blue acid”, “biker dope”, “hillbilly crack” and many other slang terms) is growing in the United States and other Western countries. It is a highly addictive synthetic stimulant that is easily and inexpensively manufactured in clandestine laboratories. Users describe a sense of euphoria, increased energy, decreased appetite, and increased concentration. Although methamphetamine has been abused for decades in the several areas of the United States, its historically regional distribution appears to have limited scientific study of its effects on the developing fetus. Antenatal methamphetamine use has been associated with prematurity, increased risk for abruption, decreased fetal growth, and intraventricular hemorrhages ^(1,2), but the medical literature on neonatal outcomes is relatively sparse compared to that of cocaine and heroin, and confounding factors are multiple. Additionally, no long-term developmental studies of fetuses exposed to methamphetamine have been published.

Because of the paucity of data, the National Institutes on Drug Abuse called for increased research in to the effects of methamphetamine abuse on the developing fetus. Alan Leshner, Ph.D., NIDA's Director from 1994 to 2001, stated that "We need to get a handle on this fast. Unless we get into this rapidly, we're going to make the same mistake we made with cocaine."⁽³⁾ The mistake Dr. Leshner refers to was the unscientific furor over "crack babies" of the 1980s; yet already, there are signs that such a furor over “meth babies” is beginning and, as in the early days of the crack epidemic, efforts are underway in at least one state (Idaho) to incarcerate pregnant methamphetamine abusers.

Though long term methamphetamine studies are lacking, existing human and animal studies provide ample reason for concern. Animal studies using sheep and rodents have demonstrated that maternal and neonatal use of methamphetamine during pregnancy can decrease uterine blood flow, decrease fetal PaO₂ ⁽⁴⁾, cause poorer maternal post-partum care of rat pups ⁽⁵⁾, decrease fetal growth ⁽⁵⁾, alter learning ⁽⁶⁾, and increase rates of malformations ^(7,8). While several human studies also suggest an association between prenatal methamphetamine exposure and decreased fetal growth ^(1, 2, 9, 10), a recent larger study did not find a significant difference in mean head circumference, length, or weight. This larger study found that methamphetamine-exposed infants were significantly more likely to be small for gestational age (defined as length, head circumference, or weight less than 5%)⁽¹¹⁾. Interestingly, this larger study also found that antenatal smoking in combination with methamphetamine resulted in a significant decrease in birth weight and head circumference (but not length).

Like cocaine, methamphetamine has been associated with hemorrhagic and ischemic strokes in adults. Only one published study, though, examines CNS imaging in neonates following antenatal use of methamphetamine. Dixon & Bejar found a variety of hemorrhagic intracranial lesions in a relatively small group (n = 24) of term infants exposed to antenatal methamphetamine ⁽²⁾. Smith, Chang, and others examined MRI and MRS results of children exposed prenatally to methamphetamine and found smaller subcortical volumes and altered creatinine levels in the striatum as well as decreased performance in a variety of attentional-based tests ^(12, 13). Smith also found that withdrawal symptoms (by "Finnegan" scores) were present in 49% of meth-exposed infants, but only 4% required treatment, suggesting that the symptoms are not as pronounced as in narcotic withdrawal ⁽¹¹⁾.

Much about the antenatal effects of this drug remains to be determined. Large studies linking methamphetamine to malformations are completely lacking and its human teratogenic potential at this time

cannot be substantiated. While it is plausible to link maternal methamphetamine to a variety of neonatal morbidities (supraventricular tachycardia, bowel infarctions, and others), no published studies have yet supported this link. Additionally, Oro & Dixon suggest that the withdrawal state characterized by agitation and poor sleep is actually an intoxication that is followed by true withdrawal, manifesting as poor feeding requiring gavage and decreased wakefulness ⁽¹⁾.

The studies discussed herein highlight the truly critical need for controlled long-term developmental studies of infants exposed antenatally to methamphetamine.

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ANIMAL MODELS OF FETAL METHAMPHETAMINE PHYSIOLOGY

Stek AM, Baker RS, Fisher BK, et al. **Fetal responses to maternal and fetal methamphetamine administration in sheep**. AJOG. 1995; 173(5):1592-1598.

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Stek et al. at the University of Cincinnati investigated the maternal and fetal cardiovascular effects of methamphetamine ingestion near term by pregnant sheep, followed by a dose-response study examining administration of methamphetamine to the pregnant ewe as well as directly to the fetus. After placing central lines in both ewe and fetus, the animals recovered for at least 5 days prior to administration of increasing doses of methamphetamine (0.03, 0.1, 0.3, and 1.0 mg/kg) to the mother via slow IV bolus. On a different day, the fetus received increasing doses of methamphetamine based on estimated fetal weight (0.03, 0.1, 0.3, 1.0, and 3.0 mg/kg). Measured variables included maternal and fetal blood pressure, left and right uterine arterial blood flow, umbilical arterial flow, and maternal and fetal blood gas analysis. Uterine vascular

resistance and umbilical vascular resistance were also calculated.

As expected, maternal administration of methamphetamine caused a statistically significant dose-related increase in maternal blood pressure that peaked 5 minutes after injection. At the 1 mg/kg dosing level, maternal blood pressure increased 76% from a baseline of 82 +/- 3 mm Hg to 130 +/- 8 mm Hg. Uterine vascular resistance increased in all animals after maternal dosing, to a maximum of 140 +/- 31% over baseline, reaching statistical significance at the 0.3 and 1 mg/kg doses. The mean uterine blood flow dropped by 19% (not statistically significant). In response to maternal methamphetamine, fetal mean arterial pressure demonstrated a progressive dose-related increase up to 28 +/- 3% over baseline (1 mg/kg dose). In contrast to uterine blood flow, umbilical blood flow increased by 15 +/- 7% over baseline ($p = 0.05$). Fetal blood gas analysis demonstrated a statistically significant progressive fall in fetal PaO₂. At the 1 mg/kg dosing level, fetal PaO₂ fell from a baseline of 21.2 +/- 1 mm Hg to 16.3 +/- 2.2 mm Hg ($p = 0.01$). Fetal pH and PaCO₂ did not change significantly. Administration of methamphetamine directly to the fetus also produced a large increase (40 +/- 1%) in fetal mean arterial pressure and a significant drop in pH (from 7.30 at baseline to 7.157 +/- 0.085 ($p = 0.05$)), but it did not produce a significant change in either PaO₂ or PaCO₂.

While the authors caution that significant differences exist in the uteroplacental unit between sheep and humans, this study provides a basic model for examining the key fetal physiologic effects of methamphetamine. According to the authors, the doses used are similar to those typically consumed by humans (0.2 to 2 mg/kg) and fetal methamphetamine levels were approximately 65% of maternal levels, indicating substantial placental transfer. Impressive dose-related changes in multiple variables were evident, including progressive increases in uterine vascular resistance and fetal and maternal MAP as well as a progressive fall in fetal PaO₂. These findings, particularly the progressive fetal hypertension and progressive increase in uterine vascular resistance, provide potential explanations for two reported perinatal methamphetamine complications: neonatal intracranial hemorrhage (discussed below) and placental abruption. The authors concluded that the fall in fetal PaO₂ was likely due to compromised uterine blood flow. The study is also valuable in demonstrating that high doses of methamphetamine (administered directly to the fetus) can cause a marked acidosis. Although a mild elevation of fetal PaCO₂ was detected following direct administration of methamphetamine to the fetus, the degree of the acidosis implies compromised metabolism resulting in lactic acidemia, a finding previously reported (Dickinson JE, Andres RL, Parisi VM. [The ovine fetal sympathoadrenal response to the maternal administration of methamphetamine](#). Am J Obstet Gynecol. 1994; 170(5 Pt 1):1452-7). While the study provides attractive basic physiologic data regarding the transfer of methamphetamine and its effects on the maternal and fetal circulation, it did not fully model prolonged human methamphetamine use.

NEONATAL INTRACRANIAL HEMORRHAGES

Dixon SD and Bejar R. **Echoencephalographic findings in neonates associated with maternal cocaine and methamphetamine use: Incidence and clinical correlates**. J Pediatr. 1989; 115(5):770-778.

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Cocaine and methamphetamine, substances with strong cardiovascular toxicities, have been associated with hemorrhagic and ischemic strokes. Suzanne Dixon and Raul Bejar at UCSD examined cranial ultrasounds of healthy term infants exposed antenatally to illicit stimulants in comparison to both healthy term and ill term controls.

Group 1 consisted of clinically healthy "exposed infants" in the newborn nursery identified by positive urine drug screens. These 82 infants consisted of 37 cocaine-exposed, 27 methamphetamine-exposed, and 18 infants exposed to a stimulant plus a narcotic (heroin and/or methadone). Group 2 consisted of 87 ill term (> 37 weeks) infants at risk for neurologic damage due to common neonatal illnesses (asphyxia, meconium aspiration, severe sepsis ($n = 12$), etc). Group 3 consisted of 19 randomly selected healthy term neonates. Infants underwent a cranial ultrasound within 3 days of birth, which was read twice by interpreters blinded to the toxicology screen results. Additionally, neonatal abstinence scores ("Finnegan" scores) and growth parameters were recorded.

Although this study examined infants exposed to other drugs (cocaine and opiates), subgroups were defined a priori. Major differences were present in group demographics, prenatal care, infant growth parameters, maternal gravity and parity, and the percentages of infants in each group that were small for gestational age and subject to intrauterine growth restriction (see discussion below regarding fetal growth). Overall, 35% of the drug-exposed infants (Group 1) had abnormal cranial ultrasound results, similar to the rate of abnormal ultrasound findings in term, ill infants at risk for neurologic damage (Group 2). Ultrasound findings were classified as white matter cavities, white matter densities, acute infarctions, intraventricular hemorrhage (IVH), subarachnoid hemorrhage, subependymal hemorrhage, and ventricular enlargement. The table below details the findings:

	Methamphetamine-Exposed (n=24)	Cocaine (n=32)	Stimulant + Narcotic (n=18)	Group 2 (ill infants at risk for neurological damage) (n=87)
White matter cavities	1 (4.2%)	5 (15.6%)	0	0
White matter densities	3 (12.5%)	4 (12.5%)	0	8 (9.2%)
Acute infarction	0	2 (6.3%)	0	4 (4.6%)
IVH	4 (16.7%)	4 (12.5%)	1 (5.6%)	5 (5.7%)
Subarachnoid Hemorrhage	4 (16.7%)	4 (12.5%)	2 (11.1%)	9 (10.3%)
Subependymal Hemorrhage	3 (12.5%)	4 (12.5%)	1 (5.6%)	3 (3.4%)
Ventricular Enlargement	2 (8.3%)	4 (12.5%)	1 (5.6%)	6 (6.9%)


The 19 infants in the healthy control group (Group 3) all had normal cranial ultrasounds with the exception of a single infant with a subependymal hemorrhage. For statistical analysis, methamphetamine-exposed infants were grouped together with cocaine-exposed infants. While the overall incidence of intracranial ultrasound abnormalities was statistically similar between drug-exposed and the ill term infants, the exposed infants had significantly more abnormalities than the healthy control group. The overall incidence of IVH was 12.1% in drug-exposed infants while only 5.7% in ill term newborns, and absent in controls ($p < 0.0001$).

This study, the only one of its kind, suggests that apparently healthy full term infants exposed to stimulants have a relatively high risk for intracranial abnormalities on neonatal ultrasound. Ultrasound with its limited window is perhaps not the ideal modality to identify some of the lesions (acute infarction and subarachnoid hemorrhages) and it is only fair at identifying white matter lesions (PVL), but it provides a good assessment of other lesions (IVH, ventricular enlargement, and subependymal hemorrhage). The numbers of infants in each subgroup are relatively small, but taken as a whole, the results of this study are thought-provoking, particularly when seen in conjunction with the animal data documenting dose-related increases in fetal blood pressure following maternal methamphetamine ingestion. Although severity was not discussed, the finding of IVH in 4 of 24 apparently healthy term infants exposed to methamphetamine is striking and suggests that ultrasound and developmental surveillance should be considered in any exposed infant.

FETAL GROWTH, PREMATURITY, AND WITHDRAWAL


Oro AS, Dixon SD. **Perinatal cocaine and methamphetamine exposure: Maternal and neonatal correlates.** J Pediatr. 1987; 111:571-578.

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Comchai C, Manorom NN, Watanarungsan P, et al. **Methamphetamine abuse during pregnancy and its health impact on neonates born at Siriraj Hospital, Bangkok, Thailand.** Southeast Asian J Trop Med Pub Health. 2004; 35(1):228-231.

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Smith L, Yonekura ML, Wallace T, et al. **Effects of prenatal methamphetamine exposure on fetal growth and drug withdrawal symptoms in infants born at term.** Dev Beh Pediatr. 2003; 24(1):17-23.

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Several studies in diverse populations have examined the effect of methamphetamine on fetal growth, prematurity, and withdrawal. Oro & Dixon examined 110 infants at UCSD Medical Center with positive maternal

or neonatal drug screens, excluding infants of mothers with histories of methamphetamine use during pregnancy but negative drug screens, and infants exposed to phencyclidine or barbiturates. The remaining infants were classified as exposed to cocaine (13), methamphetamine (28), cocaine plus methamphetamine (5), narcotics (49), and narcotics plus cocaine or methamphetamine (9). Controls (45) were randomly identified and matched for ethnicity, maternal age, and prenatal care. Tracked variables included gestational age (by Dubowitz), growth parameters and rates of SGA, withdrawal scores and treatment, and abruption rates. Because the infants exposed to cocaine and methamphetamine were statistically identical, they were grouped together for comparison with narcotic-exposed infants and controls.

More recently (2001), Comchai in Bangkok, Thailand examined methamphetamine's effect on Apgar scores, growth parameters (OFC, length, weight), prematurity, and withdrawal symptoms. Infants were included in the study group only if mothers admitted to using methamphetamine and if it was also present in the infant's urine. The control group consisted of infants born during the same period whose mothers denied methamphetamine use.

Finally, Smith et al examined fetal growth parameters and withdrawal symptoms among 134 term singleton infants exposed to methamphetamine at a large public hospital in Los Angeles County. Although infants exposed to marijuana and alcohol were included in the study group, infants exposed to narcotics (4) and cocaine (16) were excluded. The control group consisted of all live term singleton births with either negative urine drug screens or no maternal history of drug use. An interesting component of this study was the examination of nicotine's effect on fetal growth among infants exposed to methamphetamine.

Oro & Dixon, who grouped cocaine-exposed infants with methamphetamine-exposed infants into a "stimulant" group, found statistically significant decreases in birth weight, length, and head circumference relative to controls. However, the stimulant-exposed group had a higher rate of prematurity (28%) v controls (9%) and a correspondingly wide range of growth parameters, suggesting that some of the difference may have been related to premature birth. Nevertheless, the stimulant-exposed group had higher rates of small-for-gestational-age infants than controls (8.7% v 2.2%) and microcephaly (17% v 4%). While Comchai also found a trend toward decreased birthweight and length in methamphetamine-exposed infants relative to controls, only decreased OFC reached standard statistical significance. Using multiple regression analysis to control for gestational age, Comchai found that both birth weight and head circumference were significantly decreased.

In contrast, Smith's study of 134 term infants exposed to methamphetamine did not show a statistical decrease in birthweight, length, or OFC compared to unexposed term infants. When both nicotine and methamphetamine were used antenatally, however, a significant decrease in birth weight and OFC was seen relative to infants exposed to methamphetamine alone. Further, Smith found maternal methamphetamine use in all three trimesters produced a significant decrease in head circumference and weight relative to use limited to the first two trimesters. Like Oro & Dixon, Smith found that the number of small-for-gestational-age infants was statistically increased among exposed infants. Although all the infants in Smith's study were considered term, methamphetamine-exposed infants were born earlier than control infants.

Withdrawal symptoms were examined in two of these studies. Oro & Dixon found a number of neurobehavioral alterations in cocaine/methamphetamine exposed infants, including abnormal sleep (81%), tremors (71%), poor feeding (58%), hypertonia (52%), vomiting (51%), sneezing (45%), high pitched cry (42%), frantic fist sucking (42%), and others. The mean peak neonatal abstinence syndrome (NAS) score was elevated among the stimulant-exposed group (5.5 +/-2.2), but much lower than that of the narcotic-exposed group (10.7 +/-3.7). Peak symptoms were typically noted on day 2 (range 1 to 6). The authors believed that some of the symptoms could have been due to methamphetamine intoxication rather than withdrawal, as the drug was recovered from the urine for up to 7 days and the initial hyperirritable phase was in some cases followed by extreme drowsiness and need for prolonged gavage feeding (similar to methamphetamine withdrawal in adults). Similarly, Smith found that 49% of methamphetamine-exposed infants had withdrawal symptoms (defined as NAS score >5), but only 4% required treatment.

Multiple factors may contribute to decreased fetal growth, making it difficult to attribute poor fetal growth solely to maternal methamphetamine use. Studies are typically complicated by the use of concomitant illicit substances, poor maternal nutrition, alcohol abuse, difficulty in assigning accurate gestational age due to lack of prenatal care, and numerous other problems. Determining duration, timing, and amount of drug abuse is also very difficult. Some cases of methamphetamine use may have been missed in these studies because inclusion was determined by maternal report and/or urine samples without meconium screens. Nevertheless, several results of these studies deserve emphasis. Both the Oro & Dixon and the Smith studies demonstrated higher rates of small-for-gestational-age infants among neonates exposed to antenatal methamphetamine, while Smith also found that exposure to methamphetamine during all three trimesters was associated with an increased risk for growth restriction. Cigarette smoking, which is extremely common among methamphetamine users, appears to contribute significantly in decreasing fetal growth. Additionally, methamphetamine use is associated with increased rates for preterm delivery as well as earlier delivery for infants delivered at term. Finally, antenatal methamphetamine use is associated with neurobehavioral alterations in the neonatal period including sleep alteration, irritability, tremors, feeding difficulties, and others. Possibly, some of these symptoms actually represent intoxication and may be followed by a prolonged period of drowsiness and poor oral feeding similar to the depressed withdrawal state noted in adults.

Smith LM, Chang L, Yonekura ML, et al. **Brain proton magnetic resonance spectroscopy in children exposed to methamphetamine in utero.** *Neurology*. 2001; 57:255-260.

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Chang L, Smith LM, LoPresti C, et al. **Smaller subcortical volumes and cognitive deficits in children with prenatal methamphetamine exposure.** *Psychiatry Research: Neuroimaging*. 2004; 132:95-106.

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Smith & Chang et al have published two controlled studies of brain magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) of children exposed antenatally to methamphetamine for at least 2 of 3 trimesters. Their reports included limited developmental assessments, a topic receiving very little attention to date. The authors first compared MRI/MRS and Child Behavioral Checklist (CBCL) results from 12 methamphetamine-exposed (age 8.1 +/- 0.8 yr) and 14 control children (age 7.3 +/- 1.1 yr). Exclusion criteria included prematurity, developmental delays, seizures, ADHD, significant maternal illnesses, other illicit drug exposure in utero, and use of chronic medications. Levels of creatine, N-acetylaspartate, choline-containing compounds, and myoinositol were measured in the right frontal white matter and right striatum (chosen based on previous animal and adult work by the group). This was followed by a pilot study examining volumes of subcortical gray matter with MRI and neurocognitive assessments in children (age 6.9 +/- 3.5 yr, range 3 - 16 yr) exposed antenatally to methamphetamine, with a control group again consisting of children not so exposed. Some of the children in the study and control groups participated in both studies. Inclusion and exclusion criteria for the second study were the same as the first study. Within 1 month of the MRI, 10 exposed and 9 control children also completed blinded neuropsychological tests of visual motor integration, motor function, sustained attention, visual attention, memory, and others.

In the first study, MRI scans revealed no detectable gross differences. The proton NMR revealed significant increases in striatal creatine (+ 10%, $p = 0.02$) among exposed children, while levels of N-acetylaspartate, myoinositol, or choline-containing compounds were unchanged. Frontal white matter levels of all compounds were unchanged between exposed children and controls. CBCL revealed that 17% of methamphetamine-exposed children had social problems or delinquent behavior, with no problems identified in controls (not statistically significant). The second study, examining subcortical gray matter using MRI, also found no gross structural abnormalities among the exposed children, but subcortical gray (putamen, globus pallidus, caudate) and hippocampal volumes were decreased bilaterally among exposed children. Neuropsychological testing revealed statistically poorer performance among the exposed children in visual motor integration, attention and psychomotor speed, and long term spatial and verbal memory. Though not reaching statistical significance, a reduction in volume of midbrain and cerebellum among exposed children was noted as well.

Smith & Chang's studies suggest that intrauterine methamphetamine exposure is associated with persistent subtle alterations in subcortical metabolism, structure and function, leading to difficulties with attention, visual motor skills, and memory. The authors are unable to explain the etiology of the increased creatine in the brains of children exposed to methamphetamine, but note that brain creatine levels are also increased among abstinent adult cocaine users and children exposed antenatally to cocaine. Increased creatine may be seen following gliosis, a response to neuronal loss, but the authors note that increased myoinositol should have been seen if gliosis caused the observed change in creatine. It is also interesting to note that N-acetylaspartate, which falls with neuronal loss, remained unchanged between controls and exposed children. This finding contrasts somewhat with the volumetric analysis performed in their second study, which revealed decreased size of the putamen, globus pallidus, and hippocampus, suggesting neuronal loss. Reduction of size of the putamen, globus pallidus, and hippocampus are an interesting finding in conjunction with the alterations in visual motor integration, attention, and memory detected on neuropsychiatric testing.

The authors caution that their study is small and that a larger study using thinner MRI sections is needed to confirm the reductions in size of brain structures, particularly the hippocampus.

SOCIAL DYSFUNCTION AND PSYCHOLOGICAL DIFFICULTIES AMONG METHAMPHETAMINE USERS: A SETUP FOR CHILD ABUSE AND NEGLECT

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Rates of child abuse and neglect among methamphetamine users are unknown, but social services agencies are taking an increasingly aggressive approach towards child protection in areas with widespread methamphetamine abuse. Sommers et al investigated physical, psychological, and behavioral characteristics of young adult methamphetamine abusers. The study consisted of interviews with 106 adults, age 18 to 25 years in Los Angeles County, who had used methamphetamine for at least 3 months. 55 participants were in a methamphetamine treatment program and 51 users were from the community at large. Study participants underwent a structured but open-ended interview about frequency of drug use, lifestyle, health, psychological symptoms, family background, and involvement in criminal and violent behavior. Participants were also asked to describe negative psychosocial consequences in relation to methamphetamine use.

The investigators found that the majority of respondents were addicted to methamphetamine, with almost 70% using the drug daily. Average duration of abuse was 3.8 years and almost all users (97%) engaged in methamphetamine binges typically lasting 2 to 5 days (median 3 days, range 2 to 21 days). Many users rapidly increased methamphetamine frequency following initial consumption. Mean weekly cost of methamphetamine was \$136 (range \$0-800). Social dysfunction, particularly within the family was common, with 49% of respondents reporting adverse family problems due to drug use. Psychologically, respondents experienced a number of adverse effects, including depression (37%), paranoia (62%), hallucinations (38%), and irritability (79%). Investigators reported that hallucinations were common (both auditory and command-type), as was violent behavior, with 35% of respondents having committed violent acts while under the influence of methamphetamine. Males were more likely to be violent than females (38% v 30%). Of the violent acts, 61% were in domestic relationships, 17% drug related, 13% gang related, and 9% random acts. Respondents described their violent behaviors as being "out of control," "outburst of rage," and "blowing up."

This study highlights multiple risk factors for abuse and neglect by caregivers in families affected by methamphetamine abuse. Several factors are particularly worrisome for an adequate home environment for a neonate. Binges, in which large amounts of methamphetamine are consumed for a period of days, were almost universal by users in this study. Given the care needed by any child, especially a newborn, this common behavior is of obvious concern. Adverse psychological effects, particularly paranoia, depression, hallucinations, and feelings of loss of control and rage, appear to be very common among users and question the suitability of the home environment. Perhaps most concerning, violent behavior is common with the majority of violent acts committed within domestic relationships. Given these findings, active involvement of social work and Child Protective Services are very important for any neonate with antenatal methamphetamine exposure.

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Ask the Authors

LAST MONTH'S Q & A August 2006 - Volume 3 - Issue 12

Last issue, we reviewed fetal methamphetamine physiology and the effects of antenatal exposure on neonatal growth, brain structure, and neurodevelopment.



Commentary & Reviews:
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[The eNeonatal Review Team asked the August faculty a few questions.](#)



How do you accurately determine whether an infant has been exposed to methamphetamine?



While some mothers readily admit methamphetamine use, most deny any connection with the drug. Identification of methamphetamine therefore rests upon laboratory analysis. Methamphetamine has been detected in adult hair, saliva, maternal and neonatal urine, meconium, and umbilical cord tissue. Most commonly, hospitals use analysis of maternal and infant urine drug screens and meconium analysis. Each method has advantages, but no method completely rules out exposure. Urine and saliva drug screens provide rapid results, but metabolites are excreted within days of exposure, minimizing utility if the mother has been hospitalized for several days prior to delivery or if the mother abstained from use prior to birth. Meconium may be analyzed as an immunoreactive screen, but positive results must be confirmed with gas chromatography/mass spectrometry, as immunoreactive methods have high false positive rates ([Moore C, Lewis D, Leikin J, 1995](#)). Meconium is believed to be a reflection of mid to late, but not early gestational exposure. More recently, identification of methamphetamine and other drugs by ELISA and CG/MS in umbilical cord was reported ([Montgomery D, Plate C, et al, 2006](#)). The authors noted that umbilical cord testing may be useful in cases of in utero meconium passage or in the preterm infant with delayed passage of meconium.



How prevalent is maternal use of methamphetamine?



Prevalence of methamphetamine use varies geographically - many areas in the eastern United States have only limited use, while other areas, particularly in the west, have high rates - and determining prevalence of maternal use remains very difficult. A recent prospective study of mothers based in four areas of high use (Los Angeles, Honolulu, Des Moines, and Tulsa) found that 84 of 7119 (1.18%) eligible maternal/infant pairs were exposed to methamphetamine ([Smith LM, LaGasse LL, Derauf C, et al, 2006](#)). This study excluded a number of potential subjects for a variety of criteria and some exposed infants may have been missed. Mothers were protected by a National Institute of Drug Abuse certificate of confidentiality in this study, resulting in 97.6% of identified mothers actually self-reporting the drug abuse. Furthermore, gas chromatography-mass spectrometry analysis of meconium confirmed methamphetamine use in only 21 of these 84 cases (25%), suggesting that meconium analysis has low sensitivity for detecting maternal use of methamphetamine during pregnancy.

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This activity has been developed for Neonatologists, NICU Nurses and Respiratory Therapists working with Neonatal patients. There are no fees or prerequisites for this activity.

Learning Objectives • [back to top](#)

At the conclusion of this activity, participants should be able to:

- Describe the association between prenatal methamphetamine exposure and decreased fetal growth;
- Discuss the central nervous system damage, including intraventricular hemorrhage, white matter lesions, and decreased growth of subcortical gray structures, associated with fetal methamphetamine exposure;
- Identify the neurobehavioral alterations in the newborn produced by antenatal methamphetamine exposure.

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- Dr. Noguee has indicated a financial relationship of grant/research support with Forest Laboratories and has received an honorarium from Forest Laboratories.
- Dr. Lawson has indicated a financial relationship of grant/research support from the NIH. He also receives financial/material support from Nature Publishing Group as the Editor of the Journal of Perinatology.
- Dr. Lehmann has indicated a financial relationship in the form of honorarium from the Eclipsys Corporation.

All other faculty have indicated that they have not received financial support for consultation, research, or evaluation, nor have financial interests relevant to this e-Newsletter.

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No faculty member has indicated that their presentation will include information on off label products.

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