



Maternal methamphetamine use during pregnancy and child outcome: what do we know?

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'P', 'Pure', or 'Burn' are names that have become associated with potent forms of methamphetamine made in illegal laboratories in New Zealand. The dramatic increase in the use of these drugs in New Zealand has largely been associated with the young male population. However, it has become apparent that a growing number of New Zealand women are also using methamphetamine during their pregnancy. The objective of this article was to review the literature that has associated methamphetamine-use with adverse developmental outcomes.

What little we know about the effects of 'methamphetamine-use during pregnancy on the developing child' comes from animal studies, a few human studies that have a number of methodological problems, and the recent cocaine literature. Evidence from these studies suggest there are likely to be adverse developmental effects for children exposed prenatally to methamphetamine, either because of the drug *per se* or because of the environment in which these children are raised. At present, we do not know specifically what those effects will be. Therefore, to avoid making unfounded judgements about the development of infants born to mothers using these drugs during their pregnancy, further research that considers the impact of other drug use as well as the influence of the postnatal environment is needed.

Since the 1990s, there has been a dramatic increase in the use of methamphetamine in a number of regions worldwide.¹ More recently, an increased use of methamphetamine has emerged in the Asia Pacific region,¹⁻³ and in specific parts of New Zealand.⁴⁻⁶ Although the greatest increase in use has been associated with the young male population in New Zealand,^{4,6} it is now apparent that a growing number of women of child-bearing age are also using methamphetamine. This widespread use has been reflected in the dramatic increase in referrals of women who have used this drug during their current pregnancy to the Alcohol Drug and Pregnancy Team (ADAPT) at National Women's Hospital. In 2001, 10% (6/60) of the total ADAPT referrals were due to methamphetamine use and associated problems. This escalated to 59% (34/58) in 2003.

Women referred to ADAPT have a high rate of mental and physical health problems that are often related to their drug use. Some of the psychological, social, and health problems that we have already observed in mothers referred to ADAPT for methamphetamine use or dependence over the past year are reported in Table 1.

Further anecdotal reports from other antenatal departments of hospitals in the Auckland region and community midwives suggest that a much larger number of women are using or have used methamphetamine during their current pregnancy that have not come to the attention of ADAPT. The purpose of this commentary is to explore the evidence for the harm associated with methamphetamine use in pregnancy, in order to avoid a "rush to judgement" about the potential developmental outcomes of children born to methamphetamine users.

Table 1. Psychological, social, and health problems observed in mothers referred to ADAPT for methamphetamine use

Psychosocial and Health Factors	N=34
Multiple drug use/abuse including: cigarettes (33), marijuana (14), alcohol (10), opiates (6)*	33
History of not keeping appointments for antenatal check-ups	14
Mental health problems including psychotic behaviour and attempted suicide	10
Referrals to Child, Young Persons and Family Service	10
Custody issues due to unstable home environment	7
Legal proceedings pending for mother or imprisonment	5
Medical complications prenatally	4
Known history of overdose	2

ADAPT=Alcohol Drug and Pregnancy Team; *Refer to numbers of mothers using that substance.

‘A rush to judgement-the cocaine story’

In the 1980s, prenatal drug use by women in the United States became the focus of moral and public health debate when a cheap, smokeable form of cocaine, ‘crack’, became widely available. At that time, words such as ‘crisis’ and ‘epidemic’ were being used to describe the increased availability and use of ‘crack cocaine’.

Driven by public and media interest, crack cocaine became commonly associated with poor African Americans and Latinas and was often portrayed as the cause of urban deterioration, increased gang violence, drive-by shootings, the expanding underclass, and a proliferation of infants the media dubbed ‘crack babies’. ‘Crack mothers’ were represented as modern-day villains, and their substance-dependence resulted in a number of punitive outcomes, including loss of parental rights to their children because of charges of child neglect and/or abuse, loss or reduction in their welfare benefits, and even imprisonment.⁷

Although there were valid concerns regarding the health and developmental outcome of children exposed prenatally to crack cocaine, the media often portrayed so-called ‘crack babies’ as ‘damaged for life’. Media across the US ran headlines such as, ‘*Crack babies turn 5 and Schools Brace*’⁸ and ‘*Tragic end to adoption of crack baby: Couldn’t take crying anymore mother says*’.⁹ These headlines were often based on anecdotal reports and unsubstantiated findings from small and methodologically compromised studies that suggested prenatal exposure to cocaine caused brain damage and intellectual and social impairment.

Subsequent longitudinal studies that addressed the methodological shortcomings of early investigations did not find evidence of serious brain damage, nor major impairment.^{10,11} However, what they did find was a pattern of subtle, but significant neurobehavioural effects.^{12,13} In a meta-analysis, Lester et al¹⁰ found small effects of prenatal cocaine exposure on school age IQ, but even these subtle effects resulted in a 1.5-fold increase in the number of children who needed special education services at a cost in excess of \$352 million (US) per year.

It is apparent from current reports by the media, the police and substance abuse agencies, that we are at risk of ‘a rush to judgement’ regarding the effects of prenatal

methamphetamine exposure.^{5,14} However, despite the widespread use of methamphetamine worldwide, little is known about its potential neurotoxic effects on the developing child.

Prenatal methamphetamine exposure and child development

Methamphetamine is a highly addictive central-nervous-system (CNS) stimulant, and the most potent member of the amphetamine group of synthetic drugs. Methamphetamine can be injected, smoked, snorted, or ingested orally or administered anally. These drugs have acquired a number of street names such as 'P', 'Pure', 'Burn', 'Ice', and 'Crystal' that are quite often related to their purity and psychostimulant properties.

'P', 'Pure', or 'Burn' are the names given to potent forms of methamphetamine made in New Zealand in illegal laboratories.^{5,6} 'Crystal' and 'Ice' resemble tiny chunks of translucent glass or ice which can be heated and the resulting vapour inhaled. In adults, chronic high-dose use has been shown to cause a number of adverse physiological, psychological and behavioural effects including damage to cardiac, vascular and neurological systems, hostility, violence, hallucinations and paranoid psychosis resembling schizophrenia.¹⁵

All illicit drugs taken during pregnancy cross the placenta and reach the fetus.^{16,17} The effects of drugs in the fetus can be caused directly through placental transfer of the drug, or can be secondary to changes in the fetal environment. For instance, methamphetamine has been shown to have vasoconstrictive effects resulting in decreased uteroplacental blood flow and fetal hypoxia, and anorexic effects on the mother which may result in intrauterine growth retardation.¹⁸ In addition, psychoactive drugs are quite often used in different combinations. For instance, mothers receiving daily methadone maintenance in an Auckland programme continued to use large quantities of benzodiazepines, smoked more than 10 cigarettes per day and smoked cannabis regularly during their pregnancy.¹⁹

Most (33/34) of the women referred to ADAPT in 2003 were polydrug users (Table 1). Therefore, in addition to understanding the effect of prenatal exposure to methamphetamine on child development there is also a need to understand the combined impact of these drugs on physical, cognitive and emotional development.

Evidence of adverse developmental effects from animal studies

What little we know about the effects of methamphetamine-use during pregnancy on the developing fetus and child comes from three areas: animal studies, a limited number of human studies of prenatal methamphetamine exposure, and studies of prenatal exposure to other stimulants such as 'crack' cocaine.

Animal studies have found a range of physical, motor, neurotransmitter, and behavioural effects in methamphetamine exposed rats and their offspring.²⁰⁻²⁵ These results have shown that prenatal exposure to methamphetamine may cause effects such as increased maternal and offspring mortality, retinal defects,²⁰⁻²² cleft palate and rib malformations, decreased rate of physical growth, and delayed motor development.^{21,23} Neurotoxic effects of prenatal methamphetamine exposure on serotonergic neurons produce neurochemical alterations in the CNS^{20,23,25,26} thought

to be associated with learning impairment,²⁰ behavioural deficits,²⁵ increased motor activity,²¹ and enhanced conditioned avoidance responses.²³

Evidence of potential adverse developmental effects from human studies of prenatal exposure to methamphetamines

There are a few human studies but as with the early cocaine reports, these have a number of methodological problems including small sample size and results that are often confounded by maternal use of a variety of other drugs. In these studies methamphetamine use during pregnancy has been associated with an increased rate of premature delivery and placental abruption.^{27,28} Some of the methamphetamine effects reported in animal studies have also been found in methamphetamine exposed human infants. These include clefting, cardiac anomalies and fetal growth retardation.¹⁸

A high rate (35%) of cranial abnormalities was reported in a group of infants prenatally exposed to methamphetamine and cocaine.²⁹ Oro and Dixon³⁰ found that in comparison to narcotic exposed infants, methamphetamine/cocaine-exposed infants were more likely to be preterm, lower birth weight, intrauterine growth retarded, and have a smaller head circumference. In addition, they reported more fetal distress, and more neurologic and physiologic alterations in methamphetamine/cocaine exposed infants. These effects remained when maternal factors were controlled. Decreased fetal-growth related to methamphetamine exposure was also reported by Little et al.³¹ However, they did not find congenital anomalies were significantly increased in their sample of 52 women who self-reported frequent use of methamphetamines.

The only study that has examined the long-term effects of prenatal amphetamine exposure is of a sample of 65 children born to mothers who had abused amphetamines during their pregnancy in Sweden. Developmental assessments of these children have been carried out at regular intervals from birth to 14 years of age.^{27,32,33} As there was no control group in this study, comparisons were made with Swedish peers born in 1976. At birth, 1, and 4 years of age, the mean weight, height, and head circumference of the amphetamine-exposed children were below the means of their peers.

Females, but not males, were significantly shorter and lighter than their peers and remained smaller at age 10.^{27,32} At age 8, there was a significant correlation between amount and duration of amphetamine exposure prenatally and aggressive behaviour and social adjustment.³³ At age 14–15 years, their achievement in mathematics, Swedish language, and sports were statistically below those of their classmates.³² However, impaired growth and the behavioural and academic outcomes were also associated with a number of psychosocial factors related to their environment—such as stress, number of siblings, maternal alcohol abuse, and a higher number of foster care placements.

These human studies are limited in several ways, most notably by small numbers, a reliance solely on maternal self-reporting to confirm drug use, lack of control groups, and confounding with other maternal drug use and environmental factors that were associated with the developmental outcomes. However, these findings do suggest that these children may be at risk developmentally due to both the direct effects of prenatal drug exposure and the caregiving environment associated with that drug use.

Evidence of adverse developmental effects from human studies of prenatal exposure to “crack” cocaine

Another area of research that may provide some insight into the effects of prenatal methamphetamine exposure is the cocaine literature. The pharmacological properties of cocaine and methamphetamine are similar; therefore, findings from the cocaine literature may be useful in suggesting possible developmental effects. At the same time, it is important to appreciate that methamphetamine has a longer half-life and more sympathomimetic effects than cocaine. In addition, it is likely that the demographics of methamphetamine users will be different than cocaine users. For instance, there are likely to be differences in self-identified ethnicity, the kinds and combinations of other drug use, and the socioeconomic status of the mothers.

Evidence from recent studies investigating the developmental outcomes of infants exposed prenatally to cocaine may also suggest specific domains of behaviour that are likely to be affected by methamphetamine. In the neonate, research has found effects of prenatal exposure to cocaine on infant neurobehaviour.^{34,35} The most consistent findings from these studies is the effect of cocaine on state regulation.^{34,36–38} State regulation is the newborn infant’s ability to regulate his level of arousal in the face of internal and external stimulation and serves as a marker of nervous system integrity.

The infant regularly cycles through six ‘states’, quiet (deep) sleep, active (rapid-eye-movement) sleep, drowsy, alert, fussy (active), and crying. In the alert state, infants are best able to focus attention on a source of stimulation such as auditory and visual stimuli. Therefore, the infant’s availability for interpersonal interaction and learning are at their maximum in the alert state.

DiPietro et al³⁸ found that cocaine infants displayed significantly greater state transitions and shorter sleep bouts, and fussed or cried more often. Acoustic cry characteristics that reflect reactivity, respiratory, and neural control of the cry sound were also compromised by prenatal cocaine exposure.³⁹ Karmel and Garner⁴⁰ found that cocaine-exposed infants at 1 month of age did not modulate attention relative to their arousal, preferring faster frequencies of stimulation regardless of arousal condition.

Lower arousal regulation has also been observed at 3 and 4 months of age in cocaine-exposed infants.^{41,42} Effects of cocaine have also been found on attention.^{43,44} Furthermore, Jacobson et al⁴³ found lower scores related to heavy cocaine exposure on tests of recognition memory at 6 and 12 months, and suggested that these infants had difficulty modulating their arousal and attention. Several studies have also reported cocaine effects on standardised measures of motor development. Across time, cocaine-exposed infants and toddlers to 36 months have shown a general decline in motor performance.⁴⁵ At 5 and 6 years of age, cocaine-exposed children have been shown to perform more poorly than controls on tasks that require inhibitory motor control under changing circumstances.⁴⁶ The ability to inhibit such a response may be related to memory deficits, and has been related to teacher-assessed externalising behaviours in school-aged children.⁴⁷

Drug-use in context—psychosocial risk factors

There is also evidence that maternal drug use is associated with general psychosocial risk factors that may compromise child outcome apart from substance dependence

issues. Research shows a number of these factors may be more pronounced in drug-using populations and include poverty, chaotic and dangerous lifestyles, symptoms of psychopathology, history of childhood sexual abuse, and involvement in difficult or abusive relationships with male partners.^{19,43,48-52}

Pregnant women receiving treatment for drug-dependence show a high incidence of psychopathology, including affective and personality disorders, and depressive symptoms.¹⁹ For instance, a recent New Zealand study that compared the parental characteristics of infants (whose mothers were receiving methadone-maintenance treatment for their opiate dependence) with infants born to non-opiate-dependent parents found methadone mothers and fathers reported significantly more symptoms of depression, were more likely to be living on a Government benefit, had fewer years of education, and had a self-reported history of criminal behaviour that often included (paternal) arrests for violent behaviour. In addition, opiate-dependence was associated with a self-reported history of sexual and/or physical abuse and personality characteristics of sensation-seeking, with less desire to conform to societal norms.

Risk factors related to maternal psychosocial functioning and the home environment have been found to adversely affect child development independent of the mother's use of substances during pregnancy.^{13,19,53} In an intergenerational study, drug users reported having less control over their children, and those children, in turn, were seen by their parents as being more aggressive and having more behaviour problems.⁵⁴ This link between drug-using parents and disruptive behaviour in their children has important long-term consequences, as behavioural-conduct problems in childhood and early adolescence have been shown to be important precursors of adolescent drug use, delinquency, and teenage pregnancy.⁵⁶⁻⁵⁷ Thus, converging evidence from New Zealand as well as other countries suggest that there may be a double jeopardy in which these children are at risk due to the combination of prenatal exposure effects and postnatal environmental effects.

Conclusion

There is no doubt that there has been an increase in methamphetamine-use in New Zealand, and that this increase is being noted among pregnant women. Three lines of evidence (animal studies, human methamphetamine studies, and cocaine studies) suggest that there are likely to be direct effects of prenatal methamphetamine use on neonatal and early child development. The effects at birth are likely to include preterm birth, growth retardation, and (depending on the extent and combination of drugs used) there may also be neurobehavioural outcomes that reflect neurotoxic effects on the CNS.

Based on the cocaine literature, the specific developmental domains that are likely to be affected during infancy and early childhood include state regulation, arousal, attention, and psychomotor development. Finally, these children may be born to parents who are at a high risk of parenting failure due to a range of issues beyond drug-dependence that include psychological problems, low socioeconomic status, fewer years of education, a history of criminal activity, and an intergenerational history of physical and sexual abuse.

The literature reviewed in this commentary, together with the problems we are currently observing in mothers referred to ADAPT, suggest there are likely to be

adverse developmental effects for children exposed prenatally to methamphetamine in New Zealand, either because of the drug *per se* or because of the environment in which these children are raised. At present, we do not know specifically what those effects will be. However, for those healthcare providers who are responsible for the care of these infants and for those workers in special education services, identification of the specific physical, cognitive, and social-emotional needs of these children is paramount.

This will require a two-staged approach. First, to avoid a second ‘rush to judgement’ we need well-designed studies to determine if there are effects of methamphetamine on child outcome. Second, if there are effects, we need to develop effective intervention programs for the infants and their families to reduce methamphetamine-related deficits. The cost savings alone from preventing the need for special education services in school would more than pay for early intervention programs.

However, while the ‘jury is still out’ on the effects of methamphetamine, the courts may be faced with more immediate problems in protecting the safety of these children. In Rhode Island (USA), the Women and Infants Hospital established ‘VIP’—the Vulnerable Infants Program to help the court with placement decisions and treatment for drug-exposed infants and their families so that they can remain together, where appropriate. VIP is an example of how our understanding of drug abuse (as a mental health/medical illness) translates into new collaborative efforts between the healthcare community and the criminal justice system to provide treatment as well as sanctions and act in the best interest of the child.

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