# Intrauterine illicit drug exposure and neurodevelopmental outcomes for children: how current literature informs management and assessment

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## Abstract

Drug use in pregnancy is a common problem but patterns of drug use vary over time and trends in drugs used may be different in different countries. Despite the difficulties in identifying all drugs or substances that women may use in pregnancy, and what particular effects each drug will have on the developing fetus, there is a wealth of literature on the most commonly abused drugs. This article aims to provide an overview of what is currently known about the long term neurodevelopmental consequences for children who have been exposed to drugs in the prenatal period, and how this information can inform clinical management. Drugs referred to in this review include opiates and opioids, (heroin and methadone), cocaine, amphetamines (methamphetamine), ecstasy and nicotine.

**Keywords** drugs; exposure; illicit; intrauterine; long-term; neurodevelopmental; outcomes; prenatal; substance misuse

## Introduction

Substance misuse during pregnancy is a growing concern as it affects both maternal and infant health. The longer-term complications for the developing child are still coming to light with literature now available on cohorts of children studied into teenage years.

This article does not have the space to include information specifically regarding prenatal alcohol exposure. There is a strong and growing evidence that alcohol remains one of the most damaging substances to the developing fetal brain, causing impacts which often appear many years later. The extensive availability and use of alcohol in our society means that this continues to be an important, and potentially preventable problem. It must be noted however that many women who misuse drugs in pregnancy may also drink alcohol, causing an additional impact on the child. Cocaine use in particular is strongly linked with heavy alcohol consumption.

Children brought up in homes with a parent or parents using drugs may also be exposed to a number of other factors that are known to have an impact on a child's development. For instance: poor antenatal care, exposure to cigarette smoke, poor home environment, poor nutrition, poor parenting, parental mental ill-health, domestic abuse, neglect and instability of home placement. It is almost impossible to control completely for the number of confounding factors associated with drug use and the impact of poly-drug use, so determining an effect caused by a specific drug is difficult, however some linked associations are seen and there are now studies in the literature describing long term effects following exposure.

There is evidence to suggest children who have been previously exposed will have a better outcome if brought up in a nurturing home environment with stable care providers throughout their life. This places an incentive on early diagnosis and appropriate early support (together with swift resolution of Family Court procedures, and early placement where this is necessary).

## The scale of the problem

Precise estimates of the incidence of substance misuse during pregnancy are difficult. The number of children exposed is likely to be higher than reported in the literature as pregnant women often under-report drug use. In addition, cigarettes and alcohol are commonly used and may not be reported on when drug use is the immediate concern. Evidence of under reporting has been documented in many studies including The Maternal Lifestyle Study which conducted surveys of women over a 2 year period between 1993 and 1995 in four different clinical centres in America while also analysing meconium for toxicology. They identified a 66% agreement with positive self-reporting and meconium testing for cocaine, but in 38% cases where mother denied taking cocaine there was a positive result on meconium testing and this often showed that more than one drug had been taken.

A study from Glasgow in 2013 recruited mothers who were prescribed methadone during pregnancy. A confidential maternal interview was carried out and meconium of the babies tested for drugs of misuse and alcohol metabolites. The study concluded that the true extent of illicit drug use was likely to be under reported as the majority of meconium samples indicated poly-drug use, and almost one half additionally had evidence of exposure to alcohol when only about 5% of the mothers had admitted drinking excess alcohol during pregnancy. Self-reporting remains a problem because of a number of factors including: guilt, self-denial, fear of recrimination and criminal justice consequences, judgemental attitudes (family, society and professionals), patchy availability of client-appropriate services, and expectation of child-safeguarding consequences. Furthermore, probably around half of all pregnancies are unplanned, and many women taking illegal drugs may also have irregular or absent menstruation

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leading them to believe that conception is unlikely which, in turn leads to late presentation to maternity services.

## Patterns in drug misuse change over time and between countries

Trends are seen with different drugs being popular at different times. For instance, cocaine became a major drug of concern in the 1980's. Methamphetamine is now reported as one of the most common illicit drug used globally, although methamphetamine use is still relatively uncommon in the United Kingdom. While the true extent of drug misuse in pregnancy may not be known, general information on drug use in the UK is reported. Statistics for drug misuse from the Home Office 2015/2016 Crime survey for England and Wales (CSEW) report that around 1 in 12 (8.4%) adults aged 16 to 59 had taken a drug in the last year, and for young adults aged 16 to 24 this is around 1 in 5 (18.0%). In this younger age group 6.6% had taken a class A drug in the last year, equating to 407,000 young people, and this has not changed significantly since 2010. Cannabis is one of the most commonly used illicit drugs with approximately 2.5% of women in the UK admitting to using it during pregnancy and lactation.

The Global Drug Survey (GDS), 2016 polled more than 100,000 drug users in 20 countries including the US, UK, Mexico, Colombia and Germany. It found respondents from the UK had a purchase rate of 11.6 per cent of novel psychoactive substances (NPS). These substances used to be known as "legal highs" leading many to a mistaken belief that because they were legal (and relatively freely available) they weren't harmful. They previously fell outside the UK Misuse of Drugs Act (1971) because they were structurally slightly different, but produce similar effects to either cannabis, ecstasy or cocaine. Legislation changed in 2016, and the scope was widened making these drugs now illegal. There is very little information however regarding the effects of these drugs on a developing fetus and child at present.

## Neonatal period

Most babies born to drug-using women will not have any obvious symptoms in the new-born period and unless the drug use is documented this information, in relation to the future health of the baby, may be missed. Babies born to mothers taking prescribed methadone replacement will have information documented in their health records as they are likely to be monitored for withdrawal signs in the first few days of life. This information will be of importance if the child should require further assessment in the future.

Some, but not all, babies born to drug-abusing mothers will be placed in the care of the local authority because of safe-guarding concerns and will be seen early for a health assessment as part of the statutory process for Children In Care. This is an ideal time to assess immediate health and plan longer term follow-up, and to document risk factors for future neurodevelopmental difficulties for this child. For children not in the care of the local authority this information may then be missing in the child's records. Additionally appropriate information can be missed when children are adopted, and be very difficult to trace retrospectively.

Neonatal withdrawal syndromes, symptoms of withdrawal, management and short term effects of prenatal exposure is beyond the scope of this article but has been described previously in this journal (see further reading). There has been a considerable amount of research on the neonatal abstinence syndrome (NAS) however it often remains poorly managed. What is still lacking is information on longer term outcomes for children who have developed symptoms of withdrawal requiring treatment, if these children are different to those who did not require early treatment, and whether optimal treatment of withdrawal makes a difference. We make no distinction between these groups in this article although it is clearly an area for future research.

## Long-term effects of prenatal exposure to specific substances

### Cigarette smoking

The negative effects of smoking cigarettes on fetal growth are well documented with a reduction in birthweight up to 400g when compared with non-smokers, however there is little reported evidence of long term growth problems in these children. Abnormalities in lung function have been demonstrated. There is also a clear dose-dependent relationship with Sudden Infant Death Syndrome (SIDS). Associations with neurodevelopmental difficulties in children exposed include impulsivity, hyperactivity, attention problems and poorer language and reading ability. Controlling for social background has always been difficult however. We must consider these potential long term difficulties as additional or compounding factors to the effects of exposure to other substances, as cigarette smoking is extremely common in this group of mothers.

### Cannabis

Cannabis is often accepted by many as being a relatively harmless recreational drug despite a growing body of evidence that it has a detrimental impact on the developing central nervous system during childhood and adolescence. Cannabis is frequently smoked in conjunction with tobacco, introducing those additional risks, however, exposure to cannabis is independently associated with increased risk of SIDS.

Estimation of the dose of cannabis ingested is difficult for a number of reasons. Cannabis metabolites may be undetectable in the urine at 48 hours after occasional use but can be detectable for weeks in chronic use because the active ingredients are accumulated in body fat. The amount of cannabis in "a joint" will vary, and there has been much publicity in the press about newer, stronger varieties of plants cultivated.

Moreover, there is no objective definition as to what constitutes 'light' or 'heavy' use, (and the meaning of these words changes with social norms in different groups). In most studies heavy or chronic use is described as 1 joint a day or more. Light or occasional use might be around once a month to once a week. Early effects with heavy use are intrauterine growth restriction and decreased head growth. Long term neurodevelopmental difficulties are correlated to severity and timing of exposure and include visual memory, executive functioning, attentional difficulties, and children acquire language skills more slowly. Studies have shown an increased risk of delinquency at 14 years of age, and although there is an increase in depressive symptoms there is no firm association of prenatal exposure with future