Neonatal Abstinence Syndrome

Introduction

Incidence and risk factors

1. Risk factors for illicit drug use
2. Risk factors for adverse pregnancy outcomes
3. Risk factors for neonatal abstinence syndrome

Consequences

1. Tobacco
2. Alcohol
3. Amphetamines
4. Cocaine and derivatives
5. Marijuana
6. Opiates
7. Polydrug use

Diagnosis

1. Drug use in pregnancy
2. Testing of newborns
3. Diagnosis of withdrawal

Interventions

1. Antenatal care
   a. Treatment of pregnant users of illicit drugs
   b. Smoking in pregnancy
   c. Support from caregivers for pregnant women abusing drugs
2. Postnatal care
3. Pharmacological treatment
   a. Opioid withdrawal: MORPHINE REGIMEN
   b. Non-opioid CNS depressants: PHENOBARBITONE REGIMEN
   c. Management of the vomiting baby

Discharge

The Drug use in pregnancy team

Infant protection issues

Follow-Up

Key points

References

Introduction:

Pregnant women using drugs have the same anxieties and expectations as other pregnant women. All women using drugs are entitled to accurate information, and to be treated sensitively in a non-judgmental manner.

Maternal illicit drug use is a risk factor for adverse pregnancy and neonatal outcomes including preterm birth. Infants born to mothers using illicit drugs (and alcohol and tobacco) are at risk of the toxic effects of the drugs both in-utero and ex-utero; adverse pregnancy and neonatal outcomes related to the poor socioeconomic situations and lifestyle factors associated with illicit drug use; neonatal drug withdrawal; and the subsequent poor outcomes of infants reared in a socioeconomically disadvantaged environment.

The Report of the US Preventative Services Task Force 1996,1 and the monograph review by Bell and Lau 2 1995 are used as background for the content of this guideline.

Incidence and risk factors:
The incidence of illicit drug use appears to be on the increase in the Australian National Drug Strategy Household Survey (NDSHS 1998) with nearly 50% of people reporting having used an illicit drug in their lifetime and > 20% reporting use in the last 12 months. Drugs used by pregnant women (% of pregnant women surveyed) included alcohol (73.1%), tobacco (25.9%), marijuana (17.2%), and injected illegal drugs (1.3%).

1. **Risk factors for illicit drug use**: The prevalence of illicit drug use in pregnancy is highest among mothers who smoke and drink, are unmarried, are not working, who have public or no health insurance, who live in urban areas, or receive late or no prenatal care. The Australian NDSHS found that unemployed persons, persons with low educational qualifications, persons working in blue collar jobs, and persons who were never married were more likely than others to be using drugs.

2. **Risk factors for adverse pregnancy outcomes**: Adverse pregnancy and neonatal outcomes may be associated with a variety of illicit drugs. However, much of the contribution to these outcomes may be the result of problems associated with drug use, including the use of alcohol or cigarettes, poverty, poor nutrition and inadequate prenatal care. Infections associated with intravenous drug use also have an impact on the mother and infant. The incidence of hepatitis C virus infection (anti-HCV positive) in a cohort of 131 pregnant women from the methadone clinic at RPA Hospital was 95% (125/131). None of the women were positive for HIV antibodies. Of 61 women followed up, 38 (62%) had evidence of past hepatitis B infection (HepBcAb positive).

3. **Risk factors for neonatal abstinence syndrome**: Withdrawal symptoms in the neonate may occur as a result of a variety of drugs including opiates, cocaine and derivatives, amphetamines, and alcohol. With less certainty, abnormal neurobehavioral patterns have also been reported in newborn infants of mothers with high intakes of caffeine, cigarettes, marijuana and volatile substances.

   Studies have found conflicting results in their ability to relate methadone dose and severity of withdrawal. Withdrawal appears to be greater in infants born to mothers on higher doses of opiates. Withdrawal is less severe in infants of mothers taking less than 20-mg methadone a day. Withdrawal from heroin usually occurs earlier (within 24 hours of birth) and is less severe than from methadone (usually 2 to 7 days after birth).

### Consequences:

The consequences of drug use in pregnancy may be a result of the direct toxic or teratogenic effect of the drug on the fetus, drug withdrawal or toxicity in the neonate, or the lifestyle and maternal health issues that are associated with illicit drug use. The following reviews the consequences of abuse of six of the most commonly used drugs in pregnancy.

1. **Tobacco**: infants of mothers who smoke weigh less on average than infants of non-smoking mothers in direct proportion to the number of cigarettes smoked. An increased rate of fetal loss and prematurity have been documented in pregnancies of mothers who smoke although the effect was not significant in all studies. Pregnant women who stop smoking in the first trimester have babies that are of comparable size to non-smoking mothers. The long-term effects of prenatal cigarette smoking remain unclear. Infants of parents who smoke are at increased risk of SIDS.

2. **Alcohol**: The Fetal alcohol Syndrome consists of prenatal and/or postnatal growth restriction, CNS involvement, and specific craniofacial dysmorphic features. Excess alcohol use in pregnancy is associated with second trimester abortion and infants with FAS have a high incidence of premature delivery. Subtle neurobehavioral changes have been observed in infants of mothers who were moderate to heavy drinkers in pregnancy. Population based studies have cast doubt on
the relationship between light alcohol consumption during pregnancy and subsequent abnormal neurodevelopment in the infant.  

3. **Amphetamines:** Infants born to mothers using low dose therapeutic amphetamines have not had any abnormalities. Decreased head circumference, length, birth weight, increased rates of abruption, prematurity and growth restriction have been reported in pregnancies of mothers abusing amphetamines. In utero amphetamine exposure may lead to intracranial lesions including haemorrhage, infarction and cavitation lesions.

4. **Cocaine and derivatives:** Adverse pregnancy and neonatal outcomes have been reported in mothers using cocaine during pregnancy. However, a meta-analysis of studies examining the effect of cocaine use in pregnancy on pregnancy outcomes found that the independent effect of cocaine on adverse outcomes of cocaine was small, and that similar effects were seen in polydrug users whether or not they used cocaine. A meta-analysis examining the association between Sudden Infant Death Syndrome suggests that SIDS appears to be more common in cocaine-exposed infants although, again, the risk was similar to that of polydrug users.

5. **Marijuana:** use of marijuana in pregnancy does not appear to increase the risks of obstetric complications. It has been associated with reduced birth length and low birth weight. No consistent morphological abnormality has been found in infants of mothers who use marijuana. Subtle neurobehavioural abnormalities have been described in infants whose mothers are heavy users of marijuana although the relationship remains unproven.

6. **Opiates:** there has been no documented increase in incidence of congenital abnormalities in infants of opiate using mothers. However, increases in the incidences of sexually transmitted diseases, low socioeconomic status, poor environment and family instability have been reported in opiate using women, and hyperbilirubinaemia in the infants of opiate using women.

Withdrawal from maternal opiate use is present in 42-68% of infants of heroin users, and 68-85% of methadone exposed newborns. Withdrawal from heroin typically starts within 24 hours of birth, whilst methadone withdrawal usually occurs between 2 and 7 days after birth. A subacute withdrawal may persist for 4-6 months.

Seizures have been documented in 7.8% of infants born to mothers on methadone and 1.2% of infants born to mothers using heroin.

In a population based cohort study, Kandall found after controlling for known associated high-risk variables, the risk ratio for SIDS in each individual drug group (methadone, 3.6; heroin, 2.3; methadone and heroin, 3.2; cocaine, 1.6; cocaine and methadone or heroin, 1.1) was higher than in the non-drug-exposed group.

7. **Polydrug use:** Users of illicit drugs frequently use more than one drug. In a study of 267 Australian women undergoing treatment for alcohol or drug use, polydrug use was the norm. Meta-analysis of studies suggests that polydrug users have an increased risk of abnormal pregnancy outcomes, and the infants of polydrug users have an increased risk of SIDS.

**Diagnosis:**

1. **Drug use in pregnancy:** The initial diagnosis of drug use and dependence is made by a careful diagnostic interview. Important information includes the quantity, frequency, and pattern of drug use; adverse effects of drugs on work, health and social relationships; and any symptoms of dependence. Although a careful history is potentially a sensitive means of detecting drug use and abuse, a history of self-reported drug use identified only 40-60% of pregnant women with positive urine tests for drugs in US studies. Our experience at RPAH is that it is uncommon for an infant to have a significant withdrawal without a clinical history of drug or methadone use in pregnancy.
2. **Testing of newborns**: As compared with a maternal history of drug use, radioimmunoassay (RIA) of urine has a sensitivity of 52% and RIA of meconium has a sensitivity of 88% for identifying infants exposed to drugs.\(^{30}\)

The testing of pregnant mothers and their newborns should be weighed against the rights of the patient to privacy and autonomy, as well as the potential for adverse effects on employment, insurance coverage and personal relationships if confidentiality of the results is lost.\(^{1}\) In general, a sensitive and thorough history is the mainstay of diagnosis. Testing should be limited to situations of diagnostic uncertainty and should preferably performed with the consent of the mother.

Persons who use intravenous drugs should be periodically screened for HIV, hepatitis B and hepatitis C.

3. **Diagnosis of withdrawal**: neonatal abstinence syndrome is scored using an NAS score chart (a modified Finnegan Scoring System).\(^{32}\) Infants scoring 3 consecutive abstinence scores averaging more than 8 (eg 9-7-9) or \(\geq 12\) for 2 scores should be treated as detailed below. The scoring interval should be 4 hourly until the infant has been stabilised. Infants withdrawing from non-opiates frequently display similar behaviours to those withdrawing from opiates.

Withdrawal symptoms from opiates include:
- **Central nervous system**: tremors, irritability, sleep disturbance,
- **Respiratory system**: tachypnoea, nasal flare, chest recession,
- **Autonomic nervous system**: sneezing, yawning, fever, sweating,
- **Gastrointestinal system**: poor feeding, vomiting, diarrhoea.
- **Measuring movement**: a commercially available movement sensor with a high level of accuracy for prediction of need for treatment for NAS (sensitivity 92%, specificity 89%) is currently under evaluation at RPAH.\(^{33}\)

**Interventions:**

1. **Antenatal care**:

   - Management of women using illicit drugs and their infants is by community based services. The Drug Use in Pregnancy Service (DIPS) at Royal Prince Alfred Hospital co-ordinates the care of the women in pregnancy, the mother and infant after birth and ensures continuity with community based services.

   - Continuity of obstetric and midwifery care,\(^{34}\) and support from counselors\(^{35}\) is essential for effective management of substance abuse around pregnancy.

   - **Treatment of pregnant users of illicit drugs**: There are few controlled trials to guide interventions for pregnant women who use illicit drugs. Observational studies suggest that increasing the number of prenatal visits reduce the risk of low birth weight.\(^{1}\) Methadone maintenance is the usual treatment for pregnant women addicted to opiates, as withdrawal during pregnancy is potentially dangerous.\(^{1}\) and pregnant women in a supervised methadone program have better outcomes than women in unsupervised programs or using street heroin or polydrug users.\(^{36}\) However, methadone prolongs withdrawal in the infant. Infants whose mothers are on less than 20 mg/day of methadone tend not to have a significant withdrawal.\(^{8}\) This should be weighed against the increased risk of intravenous and other drug use if the woman is not on an adequate and stable dose of methadone. Tapering the methadone dose compared to methadone maintenance has not been trialled in pregnant women but results in increased use of heroin in non-pregnant oiate users.\(^{37}\).

   - All pregnant women should be advised about the potential risks to themselves and the fetus of drug use during pregnancy. A treatment plan should be developed that is tailored to the drug of use and the needs of the patient. Withdrawal of opiates in pregnancy may be harmful to the fetus and the woman should be stabilised on methadone.\(^{1}\).
Persons who continue to use intravenous drugs should be advised to use a new sterile syringe with each use, never to share or re-use equipment, use clean water to prepare drugs, to clean the injection site with alcohol prior to injection, and safely dispose of the syringes after use.1

Smoking in pregnancy: Obstetricians and midwives should ensure that information on self-help behavioural strategies for quitting smoking, prepared specifically for pregnant women, are available and accessible to all women in their care.38 Smoking cessation programs in pregnancy appear to reduce smoking, low birthweight and preterm birth, but no effect was detected for very low birthweight or perinatal mortality. Behaviourally orientated programs such as the QUIT program are cost effective.39

Support from caregivers for pregnant women abusing drugs: Clinics that offer continuity of care and which are sensitive to the social circumstances and needs of their clients have no known risks and may have important benefits for low-income mothers and their children.40 The DIPS team at King George V Hospital is integrated into the obstetric antenatal clinics. Women using opiates are referred to the Drug and Alcohol Service Methadone Clinic for stabilisation on methadone.

2. Postnatal care

An attempt should be made to identify women using potentially harmful drugs antenatally. Discussion of postnatal care can commence before the infant is born. All mothers using illicit drugs in pregnancy and their infants should be referred to the DIPS team.

NAS can produce a major disruption to mother infant attachment. Unnecessary separation of mother and infant should be avoided. Mothercraft techniques such as swaddling, settling, massage, relaxation baths and dummies can assist in settling babies and reassuring mothers. Non-pharmacological interventions shown to reduce symptoms in infants with NAS include maternal education teaching comforting and interacting techniques.41 Although waterbeds have been shown to comfort the infant,42 they are associated with an increased risk of SIDS.43 Use of rocking beds results in overstimulation of the infant.44

Regular post-natal care includes:

- **Diagnosis of withdrawal**: neonatal abstinence syndrome is scored using an NAS score chart (a modified Finnegan Scoring System).26 Infants scoring 3 consecutive abstinence scores averaging more than 8 (eg 9-7-9) or \( \geq 12 \) for 2 scores should be treated as detailed below. The scoring interval should be 4 hourly until the infant has been stabilised.

- **Transfer to the nursery** if NAS score \( \geq 8 \) for 3 scores, or \( \geq 12 \) for 2 scores. Further scoring in nursery is usually appropriate to confirm high scores are due to NAS. Transfer back when stabilised (scores < 8 for 24 hours).

- **Education of mother to administer morphine once infant has settled.**

- **Daily assessment for signs of withdrawal, adequacy of feeding, adequacy of weight gain (or severity of weight loss), assessment of mothercraft abilities of mother and monitoring for signs of continued drug use.**

- **Teaching mothers comforting and interaction techniques for use with their infants.**

- **Infants should be weighed on day 5 and 2nd daily thereafter.**

- **Encouragement of breastfeeding if the mother is stable on methadone. Breastfeeding is discouraged if the mother is on heroin or other sedatives and stimulants.**

- **Liaison with DIPS social worker and nursing staff concerning social situation and need for DOCS referral.**

- **Hepatitis B vaccine before discharge, or hepatitis B vaccine and immunoglobulin within 72**
If a baby at risk of NAS has 3 consecutive abstinence scores averaging more than 8 (e.g. 9-7-9), or ≥ 12 for 2 scores, treatment as detailed below should be commenced and the scoring interval should be 4 hourly until the infant has been stabilised.

**Opioid withdrawal:** If mother uses opioid drugs (e.g. methadone, heroin, and pethidine) +/- other central nervous system depressant drugs, morphine is the drug of choice. Morphine has been shown in a randomised-controlled trial to be better than phenobarbitone at preventing seizures in infants with opiate withdrawal\textsuperscript{45}, although it does increase the time infant stays on treatment\textsuperscript{46}.

### MORPHINE REGIMEN

Pharmacy prepares morphine as a 0.5mg/ml aqueous solution.

<table>
<thead>
<tr>
<th>NAS score (score every 4 hours)</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score averages ≥ 8 for 3 scores</td>
<td>Morphine 0.5 mg/kg/day in 4 divided doses orally</td>
</tr>
<tr>
<td>If score persists ≥ 8 despite morphine 0.5 mg/kg/day</td>
<td>Morphine 0.7 mg/kg/day in 4 divided doses orally</td>
</tr>
<tr>
<td>If score persists ≥ 8 despite morphine 0.7 mg/kg/day</td>
<td>Morphine 0.9 mg/kg/day in 4 divided doses orally</td>
</tr>
<tr>
<td>When infants are on 0.9 mg/kg/day</td>
<td>Monitor cardiorespiratory function</td>
</tr>
</tbody>
</table>

After scores fall below treatment level for 48 hrs, the dose should be reduced by 0.1ml (0.05 mg) per dose every 4 days or longer, depending on the scores. The usual length of morphine treatment is 1-2 months. Cardiorespiratory monitoring should continue for 4 days or until dose is reduced.

**Management of the vomiting baby:** ensure that the infant is not being overfed and that the infant is being appropriately postured during and after feeding. Give the morphine before the feed. If baby has a large vomit after being given morphine:

- if vomits within 10 minutes of dose, re-dose,
- if vomits after 10 minutes, give ½ dose,
- if baby vomits after feed, do not give further morphine (always err on side of caution).

### PHENOBARBITONE REGIMEN

<table>
<thead>
<tr>
<th>NAS score (score every 4 hours)</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score averages ≥ 8 for 3 scores</td>
<td>Phenobarbitone 15 mg/kg oral or IMI stat, then 6 mg/kg/day in 2 divided doses orally</td>
</tr>
<tr>
<td>If score persists ≥ 8 despite phenobarbitone 6 mg/kg/day</td>
<td>Phenobarbitone 8 mg/kg/day in 2 divided doses orally</td>
</tr>
<tr>
<td>If score persists ≥ 8 despite phenobarbitone 8 mg/kg/day</td>
<td>Phenobarbitone 10 mg/kg/day in 2 divided doses orally</td>
</tr>
<tr>
<td>When infants are on 10 mg/kg/day</td>
<td>Monitor cardiorespiratory function</td>
</tr>
</tbody>
</table>

For barbiturate withdrawal, after scores fall below treatment level for 48 hours the dose should be reduced by 2mg per dose every 4th day or longer depending on scores. For non-barbiturate withdrawal (e.g. benzodiazepines), the dose may be reduced more rapidly after withdrawal symptoms settle.
Discharge:

All mothers and infants should be assessed adequately prior to discharge by the DIPS team with respect to current drug usage and psychological stability, mothercraft abilities, social situation and the infants wellbeing.

Infants should not be discharged if:

Absolute:

- Excessive weight loss (≥ 10% of birth weight),
- Before day 5 of life,
- Suspected infant neglect or abuse,
- Suspected home violence.

Relative:

- Poor mothercraft ability of mother, and inadequate home support or acceptance of assistance,
- Erratic behaviours or continued intravenous and illicit drug use,
- Polydrug use.
- Inability of team to monitor welfare of infant.
- Mothers on high doses of methadone or other drugs should be discouraged from going home early, since their babies could withdraw at home. If such mothers insist on going home against medical advice, a DOCS notification should be considered.

The neonatal consultant on call must be notified, if parents are threatening to take their baby home with any of the above contraindications to discharge. It will usually be appropriate to admit the baby to SCBU for ongoing withdrawal observations, either voluntarily or with support from a DOCS intervention.

Home visiting and early intervention:

Home intervention in high risk families has been demonstrated to improve long term health and psychosocial outcomes in the families and children. Interventions started in pregnancy, continued to 2 years of age, used home visiting and provided continuity of care. Although promising, studies to date have not shown unequivocal benefits of home intervention of families using illicit drugs. In view of the high risk and poor follow up rates of these families, further research is needed.

Early intervention in high risk populations using daycare intervention in preschool children dramatically improves children's IQ, has beneficial effects on behavioural development and school achievement. Long-term follow up demonstrates increased employment, lower teenage pregnancy rates, higher socioeconomic status and decreased criminal behaviour. There are positive effects on mothers' education, employment and interaction with children.

The Drug Use in Pregnancy Service (DIPS)

Drug and alcohol services for pregnant women are almost entirely provided by the Drugs in Pregnancy Service based at the King George V Hospital. The DIPS was the first specialist service for drug dependent women in New South Wales, established at the Crown Street Womens Hospital in 1979 and subsequently transferred to the King George V Hospital. The service now functions as a statewide tertiary level referral and advisory service on drug use in pregnancy.

The current DIPS Team operates according to principles of harm minimisation and offers assessment and follow-up to all drug-using women who are pregnant or recently delivered. Patients receive assessment and ongoing review of their drug use problems in combination with antenatal care.

We believe that early referral enables appropriate interventions outlined by best practice models and
accounting for individual patient needs to be instituted with full awareness of the patient.

The DIPS offers assessment and follow-up of infants born with neonatal abstinence syndrome (NAS) through its morphine clinic, a clinic established to monitor clinical progress of babies on morphine treatment for opioid withdrawal. It is also accessible to clients of the DIPS whose babies do not develop NAS.

The Drug Use in Pregnancy Team consists of:

- A DIPS Social Worker,
- Paediatrician specializing in drug usage in pregnancy and the care of infants with neonatal abstinence syndrome,
- Nursing staff of K7W nursery and K7W postnatal ward,
- Neonatal early discharge team (NEDP)
- Nursing staff from Drug Health Services, CSAHS.
- Community Representation from early childhood centers, DoCS, and treatment providers and community programs specializing in the treatment of drug dependencies where appropriate.

Infant protection issues: Go to separate guideline

DOCS HELPLINE - 24 HOURS:

MANDATORY REPORTERS: 133627

GENERAL PUBLIC: 1332111

Follow-Up Neonatal Abstinence Syndrome (NAS) Clinic:

Criteria for follow up:

- All infants on morphine,
- Infants of mothers on methadone,
- Infants of mothers using frequent illicit drugs in pregnancy, and
- Any mother and her infant with significant social or mothercraft problems on a case by case basis.

The clinic consists of the Paediatrician specialising in drug use in pregnancy and the care of infants with the neonatal abstinence syndrome and the DUiP team social worker. Appointments are on Thursday afternoons and can be made by contacting the secretary on 02 9515 8760. The clinic provides the following service:

- Weekly examination of infant for signs of withdrawal, adequacy of weight gain and signs of neglect,
- Ensuring adequacy of mothercraft practices,
- Addressing all concerns of mother and family,
- Counseling by doctor and/or DUiP team social worker,
- Discussion of implications and management of hepatitis C status,
- Attending to the 6 week baby check,
- Referral to community services where appropriate,
- Discharge from the clinic when the infant is stable, off morphine, and there are no further concerns for the welfare of mother and infant.

Key Points

| Key Points | Level of Evidence |
| Drug use in pregnancy may be associated with adverse pregnancy and neonatal outcomes | 23 |
| Where appropriate, informed consent should be obtained when performing drug screens | 1 |
| All pregnant women should be counseled about the potential risks of drug use in pregnancy | 1 |
| Pregnant women reporting the use of potentially harmful drugs in pregnancy should be informed of the risks and encouraged to stop or cut down | 1 |
| Pregnant women using opiates should be stabilised on methadone | 36 |
| Patients with evidence of drug dependence should be referred to appropriate drug treatment providers and community programs specialising in the treatment of drug dependency | 1 |
| Patients injecting intravenous drugs should be counseled as to the risks of infection and in methods for preventing infection | 1 |
| Infants exposed to opiates, cocaine, amphetamines and alcohol may suffer from a neonatal abstinence syndrome | 1, 2 |
| Infants, of mothers using opiates, with an NAS score averaging ≥ 8 on 3 occasions should be treated with morphine in preference to phenobarbitone | 45, 46 |

References


49. Olds DL, Henderson CR, Jr., Kitzman H. Does prenatal and infancy nurse home visitation have enduring effects on qualities of parental caregiving and child health at 25 to 50 months of life? *Pediatrics* 1994; **93**: 89-98.


Last Reviewed: July 2001