<table>
<thead>
<tr>
<th>Title of Guideline (must include the word “Guideline” (not protocol, policy, procedure etc))</th>
<th>Guideline for the Management of Babies of Mothers with drug misuse and Prescription medications</th>
</tr>
</thead>
</table>
| Author: Contact Name and Job Title | Kumar Swamy, Specialty Doctor- NICU  
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In consultation with Neonatal Pharmacist  
Adapted from Version 5: S. Wardle, S. Watkin |
| Directorate & Speciality | Family Health, Neonatal Medicine |
| Date of submission | 14th November 2018 |
| Explicit definition of patient group to which it applies (e.g. inclusion and exclusion criteria, diagnosis) | Babies of Mothers with drug misuse and prescription medications |
| Version | 6 |
| If this version supersedes another clinical guideline please be explicit about which guideline it replaces including version number. | 5 |
| Key Words | NAS, Drug withdrawal, Neonatal abstinence |
Nottingham Neonatal Service – Clinical Guidelines                   Guideline No. F1

Statement of the evidence base of the guideline – has the guideline been peer reviewed by colleagues?

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>1</td>
<td>NICE Guidance, Royal College Guideline, SIGN (please state which source).</td>
</tr>
<tr>
<td>2a</td>
<td>meta analysis of randomised controlled trials</td>
</tr>
<tr>
<td>2b</td>
<td>at least one randomised controlled trial</td>
</tr>
<tr>
<td>3a</td>
<td>at least one well-designed controlled study without randomisation</td>
</tr>
<tr>
<td>3b</td>
<td>at least one other type of well-designed quasi-experimental study</td>
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<tr>
<td>4</td>
<td>well –designed non-experimental descriptive studies (ie comparative / correlation and case studies)</td>
</tr>
<tr>
<td>5</td>
<td>expert committee reports or opinions and / or clinical experiences of respected authorities</td>
</tr>
<tr>
<td>6</td>
<td>recommended best practise based on the clinical experience of the guideline developer</td>
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Consultation Process

Neonatal team, Drug liaison Specialist midwives, Pharmacists, Maternity governance team

Ratified by:

Neonatal Guideline consultation group

Date:

Target audience

Neonatal MDT, Midwives, Obstetricians

Review Date: (to be applied by the Integrated Governance Team)

14.11.2023

A review date of 5 years will be applied by the Trust. Directorates can choose to apply a shorter review date, however this must be managed through Directorate Governance processes.

This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date.
1. Introduction / Background

The prevalence of neonatal abstinence syndrome in the UK is approximately 2.7/1000 live births \(^1\). These babies born to drug/medication dependent mothers (drug-using mothers, mothers on long term treatments for pain or mental health conditions) are affected in some way, even if the mother has decreased usage during pregnancy.

**List of illicit and prescription drugs (list is not exhaustive)**

**Opiate** (Heroin, Oramorph, Buprenorphine, Methadone, Codeine, Tramadol, Pentazocine)

**Amphetamines** (Concerta, Equasym, Methylphenidate)

**Ecstasy/MDMA**

**Cannabis**

**Cocaine, crack cocaine**

**Gabepentin**

**Pregabalin**

**Mamba**

**Ketamine- fairly common amongst young people**

**LSD (not a commonly used drug)**

**Non-narcotic drugs, which may cause withdrawal syndrome:**

**Alcohol**

**Selective Serotonin Re-uptake Inhibitors (SSRIs)** – citalopram, sertraline, fluoxetine

**Serotonin & Norepinephrine Re-uptake Inhibitors (SNRIs)** - Venlafaxine, duloxetine

**Barbiturates** - phenobarbital, thiopental

**Bendodiazepines** - diazepam, temazepam, clobazam, alprozam

**Tricyclic antidepressants** - amitriptyline, nortriptyline, imipramine, doxapine

**Bromide**

**Diphenhydramine** - Benadryl®, Nytol®

**Glutethimide** - Doriden®, Elrodrom®, Glimid®

**Lithium**

**Meprobamate**

**Phencyclidine (PCP)**
Phenothiazines (Chlorpromazine, Promazine, Levomepromazine, Prochlorperazine)

Theophylline

1.2 Withdrawal of drugs during pregnancy

It is safe to stop amphetamines, cocaine, ecstasy, cannabis and LSD during pregnancy. It is probably safe to stop heroin and methadone during pregnancy, although this should be done as part of a controlled withdrawal programme. Alcohol, temazepam and barbiturates should not be stopped suddenly as they can result in fits.

Regarding opioid reduction, many mothers request detoxification during the first trimester. Pregnant women should be stabilised, as there is an increased risk of spontaneous abortion. Detoxification in the 2nd trimester can be undertaken in small frequent reductions (please see new orange 2017 DOH guidelines).

1.3 Effects of maternal drug use on the fetus and newborn infant

Most drug users in the UK still report opiates (primarily heroin) as their main problem drug. Local audit report for pregnant substance user reports drug users with a range of illegal drugs most commonly opiates but also a range of illicit substance including alcohol.

Please remember the use of multiple drugs. In utero exposure to polypharmacy along with opioids is associated with a twofold increased risk of neonatal withdrawal.

Opiates (heroin, methadone, and prescription opioids): Use of these drugs can result in infants being born both premature and low birth weight. These infants may show withdrawal symptoms following birth (see section 1.3). Exposure to opiates are also associated with seizures (incidence of approximately 2.7%) 2. Timing of withdrawal varies depending upon the recent history of drug dose and the half-life of drug elimination. In infants exposed to heroin (short half-life), withdrawal signs often begin within 24 hours of birth, whereas withdrawal from the longer-acting methadone or buprenorphine usually begins anywhere from 24 to 72 hours after birth. However, for both opioids, withdrawal may be delayed until five days of age or later (table 1) 3. Long term use of prescription opioids for >30 days in 3rd trimester can result in neonatal withdrawal 2.

<table>
<thead>
<tr>
<th>Opioid Drug</th>
<th>Onset (hours)</th>
<th>Frequency (%)</th>
<th>Duration (days)</th>
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</thead>
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<td>Heroin</td>
<td>24-48</td>
<td>40-80</td>
<td>8-10</td>
</tr>
<tr>
<td>Methadone</td>
<td>48-72</td>
<td>13-94</td>
<td>30 or more</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>36-60</td>
<td>22-67</td>
<td>28 or more</td>
</tr>
<tr>
<td>Opioid prescriptions</td>
<td>36-72</td>
<td>5-20</td>
<td>10-30</td>
</tr>
<tr>
<td>(Tramadol, Codeine, Oramorph)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Cannabis: Babies of mothers that use cannabis do not have signs of serious withdrawals but can result in a higher pitched cry, trembling and unexpected responses to visual stimuli. However, there is emerging evidence to suggest that cannabis exposure during the prenatal period can affect the child’s intellectual development, such as depressive symptoms, attention deficit, hyperactivity and impulsivity, lower IQ scores and difficulties on tests of learning and memory 4.

Alcohol: Heavy drinking can result in the fetal alcohol spectrum syndrome, although there are no known ‘safe level’ for alcohol consumption. The UK government recommendation is for complete abstinence of alcohol 5. Features of fetal alcohol spectrum disorder include distinctive facial features, impairment in neurocognitve functioning (impairment in global intellect, executive functioning and learning, memory impairment), difficulties in mood and behaviour regulation and impulsivity. There is
also increased risk of impairment in language and communication, motor skills and social communication and interaction. With regards to the babies born to mothers with alcohol dependency, these babies should stay in hospital for at least 24 hours with 4 hourly observations and Rivers withdrawal observation is recommended if any concerns (discuss with Drug liaison Specialist midwives).

**Amphetamines and ecstasy** ("speed", "ice", "crystal"): The use of these drugs may cause prematurity, intrauterine growth restriction and fetal demise. The risk of congenital anomalies such as cleft palate and heart defects remains unclear. In terms of withdrawal symptoms, Infants exposed to stimulants such as amphetamines have been shown to be less symptomatic compared to those exposed to opioids.

**Benzodiazepine**: 1. Long-acting forms include: diazepam, nitrazepam, flurazepam, alprazolam, chlordiazepoxide, clobazam, clonazepam 2. Short-acting forms include: lorazepam, loprazolam, lormetazepam, temazepam, oxazepam

Withdrawal symptoms of long-acting forms such as diazepam have been shown to appear within a few days and last for 3 weeks, but may persist for a few months. High doses of diazepam (>30mg) has been associated with lower APGAR scores. On the other hand, the use of oral lorazepam have not been shown to have any significant impact on full term neonates apart from slight delay in establishing feeds.

**Cocaine**: Use of this drug may be associated with placental abruption and premature rupture of membranes, increased rates of stillbirth, neonatal death and sudden unexpected death in infancy (SUDI). There may be intra-uterine growth restriction. The newborn baby may have poor feeding and can be difficult to comfort until the drug has been cleared from its system. These babies are also more likely to have central and autonomic neurological symptoms which include tremors, high-pitched cry, irritability, excess suck, hyper alertness, apnoea or tachypnoea. These acute central and autonomic abnormalities appear to be a direct effect of cocaine rather than withdrawal symptoms. These symptoms tend to appear during the 2nd and 3rd postnatal days.

**Barbiturates**: Use of barbiturates is associated with both neonatal withdrawal symptoms and congenital malformations. Symptoms may present at a median age of seven days of life (range 2 to 14 days). Symptoms include irritability, constant crying, sleeplessness, tremors, hiccups, and mouthing motions.

**SSRIs/SNRIs**: Use of selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) during pregnancy is associated with poor neonatal adaptation. This has been reported in approximately 30% of infants of mothers treated with SSRIs in the last trimester. The symptoms normally persist for 3 days, but can last for up to 2 weeks. The symptoms include temperature instability, feeding difficulty, jitteriness, irritability, sleep problems, tremors, shivering, restlessness, convulsions and rigidity. There is also an increased risk of pulmonary hypertension in these babies. Most studies indicate that SSRIs as a group are not major teratogens and are not associated with birth defects. There is insufficient evidence to show the dosage effect of these medications, however one study showed that there is no complications seen in infants whose mothers had been treated with <20mg/day of paroxetine.

**LSD, magic mushrooms**: There is no evidence that these drugs have any significant harmful effects on either the fetus or the pregnancy.
1.3 Signs and symptoms of neonatal withdrawal

These are predominantly non-specific in nature, broadly similar and do not necessarily indicate a state of withdrawal of a particular drug of dependence. If you notice any of the following it should prompt consideration of neonatal withdrawal syndrome:

<table>
<thead>
<tr>
<th>Withdrawal symptoms</th>
<th>Metabolic/vasomotor/respiratory</th>
<th>Gastrointestinal</th>
<th>CNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Vomiting</td>
<td>Tremors</td>
<td></td>
</tr>
<tr>
<td>Yawning</td>
<td>Poor feeding</td>
<td>High-pitched crying</td>
<td></td>
</tr>
<tr>
<td>Sweating</td>
<td>Excessive sucking</td>
<td>Sleep disturbances</td>
<td></td>
</tr>
<tr>
<td>Sneezing</td>
<td>Watery stools</td>
<td>Hypertonia</td>
<td></td>
</tr>
<tr>
<td>Tachypnoea</td>
<td>Weight loss</td>
<td>Irritability</td>
<td></td>
</tr>
<tr>
<td>Mottling</td>
<td></td>
<td>Seizures</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Symptoms of neonatal withdrawal

A baby is more likely to develop withdrawal symptoms if the mother has been regularly taking drugs during the later stages of her pregnancy. However, there is some evidence to suggest that even intermittent use by the mother can result in physical dependence in the foetus. A baby may show signs of withdrawal even when the mother has not recently used opiates.

2. Management

2.1 Antenatal care (see also antenatal guideline-1545)

2.1.1. Mothers who are using these drugs/medications should be informed that their baby would require observation in hospital after birth on the postnatal ward. Mothers should be offered a copy of the Rivers withdrawal chart (appendix 1) so that they may have an early understanding of what to expect

2.1.2. A record should be made of the severity and duration of the mother’s drug use in the maternity documents. Details should include any periods of detoxification, including when started and the drugs used, and the minimum and maximum drug doses that mum has taken during the pregnancy.

2.1.3 Neonatal team should be informed by the maternity team of any mothers who are on these drugs/medications in advance of delivery of her baby. Their management should be planned in the multi-disciplinary perinatal alert meeting.

2.2 Delivery

Narcan TM (Naloxone) must not be given during resuscitation to the infant of a mother who has been using opiates. This is because it can result in acute withdrawal and death. Neonatal team are not required to attend deliveries of these babies routinely as generally they don’t need extra help.

Management of infants based on maternal drug misuse

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Plan/observations</th>
<th>Duration of observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioids (all)</td>
<td>Rivers</td>
<td>4 days</td>
</tr>
<tr>
<td>Cannabis</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Benzodiazepines</td>
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<td>‘Alcohol dependency’</td>
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<tr>
<td>SSRIs/SNRIs</td>
<td>Observations</td>
<td>24 hours</td>
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</tbody>
</table>

* Subject to discharge planning
2.3 On the postnatal ward

In all cases review

1. Antenatal care plan
2. Maternal medication use and detox plan
3. Maternal serology
4. Neonatal plan according to the medication used
5. Safeguarding issues and discharge plan

2.3.1 Opioids (all)

A neonatal drug withdrawal (Rivers) chart should be completed for each baby. Observations are required on admission to the postnatal ward and thereafter 4 hourly (see Appendix). Should a delay in transfer of mother and baby from the labour ward be anticipated, observations should be commenced on labour ward. The baby should be reviewed daily by the ward paediatrician as routine for Extra-Care babies.

In the presence of mild symptoms, only supportive therapy is indicated. This includes wrapping, cuddling and nursing in a quiet, low-lit environment (where appropriate and safety permits). Maternal involvement in supportive care is an important factor in the non-pharmacological management. Other causes such as sepsis or hypoglycaemia should be considered.

It is very rare that a specific pharmacological therapy (see section 3.0) is needed. Specific therapy may be considered in the presence of a score of 6 or more on the Rivers chart confirmed by 2 observers or for convulsions. It is advisable that these patients be discussed and reviewed by a senior member of the neonatal team.

2.3.2 SSRIs/SNRIs, Tricyclics, Lithium

Infants born to mothers who are taking these medications should have 4 hourly observations of heart rate, respiratory rate and temperature for at least 24 hours, BUT does not require a neonatal drug withdrawal (Rivers) chart. These babies can be discharged safely after 24 hours. Supportive measures such as maternal reassurance, frequent infant feeding, and encouragement of skin-to-skin contact between mother and infant are usually sufficient to manage poor neonatal adaptation.

2.4 Other Measures

1. Where specific therapy for withdrawal is required, a discharge planning meeting must be held to discuss duration of stay in hospital for treatment (as there is an option of reduction programme/detox performed in the community by liaison midwives).
2. Many of these babies will have an antenatal plan and will need multi-disciplinary team working to support mother (or parents) during the postnatal ward stay and post discharge.
3. Discuss with the safeguarding midwifery team if relevant or unsure (refer to safeguarding SOP). Contact social worker if there are any emerging concerns. Referral to Social Services may be considered in infants born to drug using parents if there are any other social care issues or concerns that arise in hospital (see section on issues affecting discharge). Ideally, Social Services involvement should be considered in the antenatal period. In Nottingham there is a multi-disciplinary team called MAPLG – Multi-agency pregnancy liaison group that considers the level of safeguarding input required on all pregnant substance misusers.

Mothers who misuse IV drug use in pregnancy are at increased risk of Hepatitis. Review maternal Hepatitis B/C and HIV status (C7, C10 and C11) and immunise baby if appropriate.
3.0 Specific therapy

Pharmacological treatment is very rarely needed and should only be considered once the supportive measures have exhausted. Specific therapy may be considered in the presence of persistent score of 6 or more on the Rivers chart confirmed by 2 observers or for convulsions*. These patients should be discussed and reviewed by the attending consultant neonatologist.

If symptoms are unexplained or not in keeping with the maternal medication use and need pharmacological therapy, consider urine toxicology in the baby (generally done on day 2).

3.1 Opiate withdrawal – As stated above, most of the babies would normally respond very well to supportive measures such as wrapping, cuddling and nursing in a quiet, low-lit environment (where appropriate and safety permits).

The aim of specific pharmacological treatment is to allow sleep and feeding patterns to be as normal as possible. This is best achieved by treating the child with oral morphine. Many babies only need 1 or 2 doses, and it is important not to over-treat and prolong admission. Where regular morphine has been required, treatment should be reduced every 24 hours if severe symptoms do not persist (i.e. when with withdrawal score is <6).

Treatment day 1: 0.04 mg/kg of morphine 4 hourly
Treatment day 2: 0.04 mg/kg of morphine sulphate 6 hourly
Treatment day 3: 0.04 mg/kg of morphine sulphate 8 hourly
Treatment day 4: 0.04 mg/kg of morphine sulphate 12 hourly
Treatment day 5: 0.04 mg/kg of morphine sulphate daily

(Discuss with neonatal pharmacist as required) [8]

* If the infant has a convulsion, other causes of fits other than drug withdrawal must be considered (please refer to Neonatal Seizure guideline E10). These include hypoglycaemia, hypocalcaemia, hypomagnesaemia, infection, hypoxia and intraventricular haemorrhage. It is important to remember that the symptoms of neonatal withdrawal syndrome may mimic those of congenital thyrotoxicosis. Morphine should be considered in infants with seizures secondary to drug withdrawal and also should be treated with phenobarbitone with a loading dose followed by a maintenance dose as in the Neonatal Seizure Guideline (E10).

3.2 Benzodiazepine withdrawal – May need treatment with diazepam (see Neonatal Pharmacopeia). Once the infant has been stabilised then the dose can be slowly and steadily reduced over several weeks.

3.3 Cocaine withdrawal - Babies born to cocaine-using mothers are very difficult to settle and will often need a lot of cuddling and skin-to-skin before they can be calmed and reassured. This will involve a considerable nursing and midwifery time and the mother should be encouraged to be the main comforter to help build her self-confidence as a parent and to bond with her baby. There is no evidence for a cocaine-induced withdrawal syndrome. The behaviour of cocaine-exposed infants is probably the result of CNS manifestations of foetal cocaine effect. Abnormalities in neurobehavior have been observed to continue for up to 6-9 months. They do not respond to therapeutic treatment. Routine cranial USS is not warranted in these babies.
4.0 Breast feeding

Providing their drug use is stable, all mothers who are using drugs should be encouraged to breast feed in the same way as any other mother. Almost all drugs and chemicals are passed from maternal blood to breast milk. The amount transferred will depend upon lipid solubility, water solubility, degree of ionisation at milk pH and molecular weight. For most drugs except cocaine, only about 1-2% of maternal dose appears in breast milk. Therefore, in general, although most recreational drugs are present in breast milk the amount is too small to cause harm to the baby. Women who are HIV positive or whose HIV status is unknown (refer to guideline C11) but who may have been at risk should be informed about the risks of infecting the baby and advised against breast feeding.

Hepatitis C is found in 60% of injecting drug users. It can be transmitted by breast milk but the risk is probably very low. There is no effective immunisation against Hepatitis C. We currently advise that this group of babies can be breast fed.

Each mother should be given all the information they need to make an informed choice about breast feeding. Having made their decision, they should be fully supported by all professionals involved.

They should be advised not to suddenly stop breast feeding as this may lead to acute withdrawal in their baby, therefore to gradually wean off breast feeding.

The principles of safe sleeping and feeding must be reinforced, highlighting the risks of falling asleep with the baby at the breasts.

5.0 Planning around discharge

Referrals for appropriate levels of safeguarding will have been made for most babies where a parent or parents are using illicit substances during the antenatal period. All the known safeguarding information will be documented in the maternal computer records (Maternity Medway). If families are not known to social care and new concerns arise during the postnatal period then a referral to social care should be considered. It is important to discuss this with the parents prior to the referral.

A Discharge Planning Meeting is always recommended prior to discharging home to the care of the parent in the case of:

1) The child who is subjected to a Child Protection Plan

2) New significant safeguarding concerns have been identified

The parents should be offered treatment for their drug use if not already known to the services. If the parents wish this, they should be referred to the Nottingham Alcohol and Drug support teams

Nottingham City resident: Nottingham Recovery Network – 08000665362.

Nottingham County resident: CGL (Change Grow Live) Single point of access – 0115 8960798.

Audit points:

1. Number of babies needing observation for specific drug withdrawal
2. Babies needing admission to NICU
3. Audit of associated risk factors e.g. safeguarding, Blood born infections seizures, Outcomes of DPMs
4. Follow up plans (short term and long term)
Appendix 1

DRUG WITHDRAWAL OBSERVATION CHART

BABY’S NAME…………………………………MOTHER’S NAME …………………………………………………

BABY’S NO: ……………………………………BABY’S D.O.B. ………………………………………………………

PLEASE CHART 4 HOURLY OR WHEN NECESSARY

<table>
<thead>
<tr>
<th>IRRITABILITY WITH SCRATCHING</th>
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</tbody>
</table>

SCORE

TIME AND DATE

SIGNATURE

The presence of any one feature within any group of the listed observations would result in a total score of 1 for that group of items. Therefore, the total score possible is 10.
References


