MCN for Neonatology
West of Scotland
Neonatal Guideline

Neonatal Abstinence Syndrome (NAS)

This Guideline is applicable to all Medical, Nursing and Midwifery staff caring for babies in the hospital or community setting within the West of Scotland. Staff should be aware of the appropriate drug monographs and other applicable guidelines, which will include the immunisation guideline as well as guidelines for the management of babies born to mothers with vertically transmissible viral infections (HIV, Hepatitis B and C).

Neonatal Abstinence Syndrome (NAS) is a constellation of symptoms occurring in a baby as a result of withdrawal from physically addictive substances taken by the mother. These substances include (but not exclusively) methadone and other opioids, heroin, benzodiazepines, cocaine and amphetamines as well as caffeine, nicotine and some antidepressant agents. Almost all opioid dependent mothers smoke in pregnancy, and a significant number probably also consume excess significant amounts of alcohol in pregnancy. The majority of infants with NAS in the West of Scotland will be withdrawing from opioids ± benzodiazepines; it is not know if, or by how much nicotine and/or alcohol withdrawal also play a part. (1,2).

While the majority of cases of NAS occur in infants born to mothers with a history of substance misuse, it is also possible for a neonate to develop NAS following *in utero* exposure to opioids prescribed for the treatment of chronic pain.

Antenatal Care:

The standard management of pregnant opioid dependent women includes prescription of either methadone or buprenorphine maintenance. Buprenorphine use has been associated with less illicit drug use, higher birth weight and milder NAS, but retention within a treatment programme is less, compared to methadone. Overall, there is insufficient evidence that either maintenance treatment is superior (3,4). Maintenance treatment is prescribed to stabilise lifestyle and mothers are encouraged to reduce this medication as tolerated. Mothers recognised to have problematic illicit drug use during pregnancy are reviewed in the antenatal clinic by the social work team and their care is coordinated by the SNIPs team.

At approximately 32 weeks' gestation a multi-disciplinary care planning meeting will be arranged with the aim of performing an assessment of risks to the unborn child and drawing up a family support plan. If a post-birth conference is deemed appropriate, ideally this should be held within 5 days of birth (*see discharge section)*.

Delivery:

Delivery of an infant of an opioid dependent mother is not in itself an indication for paediatric attendance. It is generally recommended that the use of naloxone (Narcan) be avoided to prevent the abrupt onset of withdrawal, but this is based on very little evidence and naloxone should be considered in any infant with significant respiratory depression at birth thought to be attributable to maternal opioid prescription. Late prematurity and low birth weight are more common in this group of babies (1).

Post-Natal Care:

Infants at risk of NAS should be nursed in the postnatal ward with their mother unless any specific indication for admission to SCBU is present. Mothers should perform all routine care, allowing the midwifery team to assess their parenting skills.

Audit (at Princess Royal Maternity) indicates that the single most important predictor of the infant developing significant NAS (and thus requiring pharmaceutical treatment) is the prescribed maternal dose of methadone at delivery. In Glasgow, the median dose of methadone at the time of delivery is around 30 - 50 mg. Higher doses of methadone are associated with polydrug use, and it is likely that pharmacogenetics also play a role (5). It is not possible to predict the development of NAS in individual babies, and so babies should generally not be discharged home before the 5th day. In order to avoid separation of mother and baby, those mothers of babies receiving treatment for NAS should be accommodated in the postnatal wards or in a designated transitional care area for up to 10 days, and occasionally longer in individual cases (6). Occasional use of cannabis, or single dose antidepressant use should not normally require 5 days' monitoring postnatally,

Breastfeeding

Breastfeeding for opioid dependent mums is associated with a 50% reduction in the risk of the infant developing NAS requiring treatment and is strongly encouraged (1). Morphine, methadone and buprenorphine administered to mothers are excreted only in small amounts in breast milk and is considered safe for breast feeding mums. It should be noted that, very rarely maternal codeine (which is metabolised to morphine) can result in neonatal morphine toxicity; codeine should be avoided, or only administered with caution in breast feeding mums (7).

Similarly, breast feeding should be encouraged in mothers prescribed SSRIs, particularly if the infant appears unusually irritable.

Cocaine and amphetamines taken during breastfeeding can cause neonatal toxicity, although this is not well understood. All mothers should be advised to abstain from stimulant drugs during lactation, and when stimulant use is identified, the baby should be closely monitored.

Mothers who are HIV positive should be advised that formula feeding is the safest way to feed their baby, although breastfeeding is possible in low risk cases (see HIV guidance)

Diagnosing NAS:

Signs and symptoms of NAS include excessive irritability, in-coordinate sucking, vomiting and diarrhoea and poor weight gain. Rarely, convulsions may occur. The diagnosis of severity of NAS (and the need for pharmaceutical treatment) is largely subjective, but various scoring systems have been used in an attempt to standardise treatment. This guideline uses the modified Lipsitz scoring system (8) to guide treatment decisions. The aim of treatment is to control symptoms to allow oral feeding, tolerable irritability and adequate weight gain. It is important that scoring is undertaken by neonatal nurses and/or midwives who have been fully trained in the method, (N.B. training requirements are determined locally).

Babies are scored twice daily, at approximately the same time (see scoring tool below).
Ad hoc scoring outside this schedule is discouraged. (It must be borne in mind that a hungry baby will easily achieve a higher score).
Aim to perform the score approximately 30-60 minutes after a feed.
Do not wake a sleeping infant to score or perform during a bath or after a procedure.

NAS is the likely diagnosis in an infant who demonstrates the signs and symptoms listed above and whose mother was known to have used addictive substances in pregnancy, but other diagnoses should be considered. Other common causes of excessive irritability can generally be excluded by careful history taking, clinical examination and/or measurement of blood sugar, calcium and magnesium. The

need for neonatal blood tests should be considered on an individual basis, but is not strictly necessary in an infant with typical signs of NAS whose mother was known to have used opioids in pregnancy, and who responds well to treatment (see below).

Modified Lipsitz Score Tool

Signs	0	1	2	3
Tremors (muscle activity of limbs)	Normal	Minimally increased when hungry or disturbed	Moderate or marked increase when undisturbed; subside when fed or held snugly	Marked increase or continuous even when undisturbed, progressing to seizure-like movements
Irritability (excessive crying)	None	Slightly increased	Moderate to severe when disturbed or hungry	Marked even when undisturbed
Reflexes	Normal	Increased	Markedly increased	
Stools	Normal	Explosive, but normal frequency	Explosive, more than 8 per day	
Muscle tone	Normal	Increased	Rigidity	
Skin abrasions	No	Redness of knees and elbows	Breaking of skin	
Respiratory rate / minute	< 55	55-75	76-95	
Repetitive sneezing	No	Yes		
Repetitive yawning	No	Yes		
Vomiting	No	Yes		
Fever	No	Yes		

Adapted from Lipsitz et al. *Clin Pediatr* 14:592-594, 1975.

Management of NAS:

Simple measures to control symptoms of NAS include swaddling, the use of dummies and prolonged nursing. The pharmaceutical treatment of choice is the substance from which the infant is withdrawing.

1. Exclude other diagnoses by careful history taking and clinical examination.

2. Document maternal drug history as accurately as possible – this should be assessed in conjunction with the mother herself, with midwifery staff and with the results of maternal urine toxicology (preferably in late pregnancy). Where the diagnosis is in doubt, a sample of infant urine may be helpful – this should be obtained as soon as possible after birth. Analysis of infant urine must be discussed with the mother, but formal consent is not required if such a test is deemed in the baby's best interests (*i.e.* to inform treatment, or in the case of unexplained seizures). Discretion is important in discussing such testing with the mother; this should not be undertaken in public, or in the presence of her partner or other family members.

3. Infants displaying signs consistent with NAS who are also at risk of hypoglycaemia must have their blood sugar measured, and if the infant does not respond to treatment within 24 hours, or if there are any atypical clinical features, plasma calcium, phosphate and magnesium should be measured. The threshold for measuring plasma biochemistry should be low and **it is important that results of any blood tests are reviewed promptly and documented.**

Treatment of NAS:
Treatment should be started if the infant is felt to be unduly irritable and difficult to console, and the Lipsitz score is ≥ 5 on two occasions 12 hours apart despite swaddling and prolonged nursing +/- the use of a dummy. Treatment may also be required if the symptoms are sufficient to cause poor feeding and/or ongoing weight loss after 5 days. The Lipsitz score must be interpreted with care in an infant with a co-existent respiratory illness. A single high NAS score must be interpreted with caution; the decision to start treatment must take into account the baby's clinical condition as well as the scoring, and should follow discussion with middle grade or more senior paediatrician.

Infants considered to require treatment for NAS should be reviewed by a middle grade doctor or ANNP prior to starting treatment, and midwifery staff caring for the baby in a postnatal ward or transitional care facility must be familiar with prescribing, dispensing and administering oral morphine solution.

There are increasing studies in the literature comparing sublingual buprenorphine to oral morphine for treatment of opiate withdrawal. Some of these studies suggest a reduction in length of treatment and hospital stay with sublingual buprenorphine, although surveys suggest that > 80% of neonatal units still use oral morphine or methadone as first line treatment. Limitations of these studies include being single centred and non-blinded and there is overall insufficient evidence to determine safety of buprenorphine in the neonatal population. We therefore still recommend oral morphine as first line treatment for opiate withdrawal at present.

Pharmaceutical treatment:
This will depend upon the mother's drug use during pregnancy. Mothers will fall into 3 groups:
A. Opiate/opioid use only (legally prescribed or illicit)
B. Opiate/opioid plus benzodiazepine +/- other substances of misuse
C. No history of opiate/opioid use

Groups A and B (opiate/opioid use)

Initial therapy - oral morphine solution 60 micrograms/kg four hourly

Escalating treatment - if symptoms are not controlled within 24 hours

• Increase oral morphine daily by 10 micrograms/kg per dose to a maximum of 80 micrograms/kg/dose

• If symptoms are not controlled after 48 hours on the maximum dose of oral morphine add **Phenobarbital** (dose as below)

Group C (no history of opiate/opioid use)

Initial therapy - start oral phenobarbital **–** loading dose 15 mg/kg, followed by maintenance dose 8mg/kg once daily (maintenance dose generally prescribed in the evening). Note that it may take several days for symptoms to come under control after phenobarbital has been commenced.

Weaning treatment:
Weaning of treatment should be commenced when the symptoms of NAS are adequately controlled. This may be defined as a Lipsitz score of < 5 on at least one occasion in the past 24 hours. Symptoms may also be considered controlled if the infant is able to be consoled (even if lots of nursing required) and is sleeping for periods of at least two hours between feeds. Weight gain is also a good indicator of resolving NAS.

Babies on oral morphine only

Each day, wean the oral morphine by 10 micrograms/kg per dose.

If symptoms worsen (scores ≥ 6) during the weaning process, review the maternal drug history and consider addition of oral phenobarbital rather than stopping or reversing the weaning of the morphine therapy. The aim is to reduce and stop the morphine therapy within the first 10 days of life to avoid admission to the NNU.

Babies on oral morphine and phenobarbital

Each day, if scores remain < 5, wean the oral morphine by 10 micrograms/kg per dose.

Oral morphine should be weaned completely before reducing the phenobarbital therapy. Once the morphine has been discontinued the phenobarbital may be weaned in hospital or, if the there are no other reasons for the baby to remain in hospital, as an out-patient.

Weaning Phenobarbital

In-patient – If it is anticipated that the baby will remain in hospital for some time then weaning the Phenobarbital dose may commence as an inpatient. Wean Phenobarbital by 2 mg/kg every two days if symptoms are controlled (scores < 5). Weaning may be accelerated if the baby is felt to be unduly sedated.

Out-patient - If home circumstances permit, consideration may be given to discharging the infant home on phenobarbital. This should be sanctioned by a consultant and regular review (1-2 weekly, depending on social circumstances and clinical stability) organised. Review may appropriately be either in a hospital outpatient clinic, or at home, by the community liaison team. (This will be determined locally) Speed of weaning of phenobarbital will depend upon symptomatology, but it is rare for babies to require treated for more than six weeks in total. A suggested initial weaning regime is a reduction by 25% of the original dose; please refer to local advice.

NB – the phenobarbital should be prescribed as a hospital out-patient prescription (50 mg in 5 ml solution). Note that the phenobarbital solution available in community pharmacies is a different strength (15 mg in 5 ml) and is not suitable for these infants. Phenobarbital is a controlled drug and the script must fulfil requirements for a controlled drug prescription. Ask advice if you are not sure!

Criteria for Admission to SCBU for the treatment of NAS:

1. Poor feeding requiring placement of a nasogastric tube.
2. Mother discharged before infant ready for home.

Hepatitis B/C Policy:

Hepatitis B: Following the introduction of Hepatitis B vaccine to the routine childhood immunisation schedule, (includes all infants born on, or after, 1st Aug 2017), it is no longer necessary to offer Hepatitis B vaccination using the accelerated schedule unless the mother is infected with Hepatitis B. A single dose of monovalent Hepatitis B vaccine is indicated at birth if another member of the household is known to be positive for Hepatitis B. In either of these circumstances please refer to the West of Scotland Immunisation guideline for details of management.

Hepatitis C: Approximately 50% of opioid dependent IV drug misusing mothers in the West of Scotland are hepatitis C antibody positive, of whom 60 – 70% (roughly 1/3 of all opioid dependent mothers) are PCR +ve (1). Vertical transmission of hepatitis C occurs in around 4-5% of cases of hepatitis C antibody +ve, PCR +ve women; this rate of infection is doubled by co-existent HIV infection. Rates of vertical transmission in hepatitis C antibody +ve, PCR -ve cases are much lower.

Mothers who are known to have injected drugs should have been offered testing for Hepatitis C during pregnancy. Babies born to mothers who are hepatitis C PCR +ve should be notified to the Infectious

Disease team at RHC who will arrange testing for Hepatitis C antibodies at a year of age. Please refer to the West of Scotland Hepatitis C guideline for details of management. There is no specific treatment in the neonatal period to prevent hepatitis C transmission, and hepatitis C infection is not a contraindication to breast feeding. Testing may be deferred to 18 months if the infant is also being followed up for perinatal HIV exposure, to minimise blood sampling.

It is important that the Badger notes and any other discharge correspondence documents if the child is known to have been hepatitis C exposed, and if mother has agreed to follow up.

Discharge Planning:

All parents with substance misuse problems who are identified during pregnancy, should have a named social worker allocated to their care. The name and contact details of this social worker must be recorded in the mother's electronic patient record. A pre-birth case discussion should have taken place during the pregnancy and an interim plan made for the care of the child. Following birth, and prior to discharge from hospital, the pre-birth plan must be reviewed, often as part of a formal post-birth case discussion. Where substance misuse is only identified post delivery this process should take place as soon as possible, and must be undertaken prior to hospital discharge. The named social worker must state that they are happy for the child to be discharged to the parent(s) **before** the baby goes home, and this **must** be documented in the notes. Any additional arrangements (e.g. mum to live with grandmother etc.) that are put in place to ensure the ongoing safety of the child should also be recorded in the baby's notes. Ideally this decision and information should form part of a written report from the social work team to be filed in the notes. If concerns regarding parental behaviour or ability to care for the child arise between birth and discharge, it is important that these are documented clearly in the nursing and medical notes and are communicated to the social work team. Such communication may either be as a statement to a post birth case discussion or as a written report, but should **not** be by word of mouth alone. Every effort should be made to predict the infant's discharge so that arrangements can be made well in advance, particularly if the child is to be discharged to foster care. Foster carers should meet with nursing staff prior to the infant's discharge so that any care needs can be discussed and/or anxieties dealt with. If the infant is discharged home on medication, this information must be given to the GP *before* discharge and prompt follow up arrangements made at the paediatric OP clinic (discuss with consultant).

Importantly, both parents and foster carers need to be aware that babies recovering from NAS can be very challenging to care for. They may demand large quantities of milk, and should generally be fed to appetite. In particular, the use of "hungry baby milks" should actively be discouraged.

Following discharge it is important to let the named social worker know promptly if the parents do not comply with the management plans outlined in these discussions (*e.g.* failure to attend clinic visits, failure to administer medication correctly), or if there are concerns over the care of the child (e.g. parents attending clinic under the influence of alcohol or drugs, or any signs of abuse or neglect)

At time of discharge:

• Inform social work department that baby is being discharged.

• Document contact details for the family as well as (if relevant) details of the foster carer and foster GP.

• Check that consent has been obtained for hepatitis C follow up, if relevant, and ensure referral sent to the ID team at RHC (mother hepatitis C PCR +ve).

• If the baby has been discharged to foster care, inform the Looked After and Accommodated Children and Young People Health Team (local contact details will differ) The LAAC team should be sent a copy of the discharge letter and copies of subsequent clinic letters.

• Ensure that follow up arrangements have been made (unless there has been a consultant decision that the infant does not require follow up). Please refer to local policy for follow up.

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