

# **NATIONAL GUIDELINE ON MANAGEMENT OF NEONATAL ABSTINENCE SYNDROME**



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**List of abbreviations:**

EMR:	Electronic medical record system
FPU:	Family protection unit
HIV:	Human immunodeficiency virus
IUGR:	Intra-uterine growth retardation
IV:	Intravenously
NAS:	Neonatal abstinence syndrome
NICU:	Neonatal intensive care unit
PNC:	Post-natal care
PPHN:	Persistent pulmonary hypertension of the newborn
SNRI:	Serotonin norepinephrine re-uptake inhibitors
SSRI:	Selective serotonin re-uptake inhibitors
TCA:	Tricyclic antidepressants

## 1. INTRODUCTION

Neonatal Abstinence Syndrome (NAS) is a constellation of symptoms evident in babies, born to mothers who are opiate-dependent and on other drugs associated with withdrawal symptoms, as babies become dependent on those drugs because of exposure during pregnancy.

The neonatal abstinence syndrome can occur in 55-94 % of newborns whose mothers were addicted to or treated with opioids/other drugs while pregnant.

*In utero* exposure to heroin and methadone has been associated with a 60% to 80% incidence of NAS. Buprenorphine has been suggested to be associated with a lower risk of NAS

## 2. AIM OF GUIDELINE

The purpose of this guideline is to ensure that babies born to mothers who are substance abusers, or who are being prescribed medications known to potentially cause withdrawal in neonates, are identified and managed appropriately without unnecessary separation from their mothers.

## 3. SCOPE OF GUIDELINE

The guideline applies to all neonates, born in maternity units in the Maldives, whose mothers are known to be substance abusers or on prescribed drugs with a potential to cause neonatal abstinence syndrome.

### 3.2. Drugs which may cause withdrawal:

- Opiates – e.g. codeine, diamorphine (heroin), methadone, fentanyl, buprenorphine, tramadol
- Benzodiazepines – e.g. diazepam, temazepam, clonazepam
- Barbiturates – e.g. phenobarbital amphetamines
- SSRIs – e.g. sertraline, citalopram, fluoxetine, venlafaxine
- Antipsychotic medications e.g. quetiapine

### 3.3. Drugs which may cause other health concerns in the infant:

- Cannabis – growth restriction, long term neuro-behavioural problems
- Cocaine – subependymal hemorrhage and cyst, vasoconstrictive effects on developing brain which may lead to neurological abnormalities
- Alcohol – fetal alcohol syndrome

### 3.4. Drug use during pregnancy can also be associated with:

- Premature labour, placental abruption, stillbirth, neonatal death (especially with cocaine abuse)
- Birth defects: cleft lip / palate (heroin/opiates)
- Underdeveloped limbs (cocaine) Intrauterine growth restriction (IUGR)
- Meconium staining of liquor
- Delayed onset of respirations / respiratory depression
- Longer term problems include sudden infant death syndrome, neurodevelopmental delay, behaviour and social problems.

In the Maldives, brown sugar (heroin) was the most-commonly used substance, followed by alcohol, opioids and cannabis. (Situational analysis of drugs in the maldives, 2021).

## 4. RECOGNITION AND ASSESSMENT

### 4.1. Aims

- To identify withdrawal symptoms following birth
- To give effective medical treatment where necessary
- To promote bonding and facilitate good parenting skills
- To support and keep baby comfortable during withdrawal period
- To optimise feeding and growth
- To identify social issues and refer to appropriate agencies

### 4.2. Clinical features

Clinical features may vary with:

- Type of drug (record accurately all maternal drugs)
- Dose of drug taken
- Chronicity of use (record last known doses)
- Timing of the last dose
- Gestational age (Term infants tend to have longer duration of symptoms)

**Minor signs**

- Tremors when disturbed
- Tachypnea (>60/min)
- Pyrexia
- Sweating
- Yawning
- Sneezing
- Nasal stuffiness
- Poor feeding
- Regurgitation
- Loose stool
- Sleeping <3 hr after feed (usual among breastfed babies)

**Major signs**

- Convulsions
- Profuse vomiting or diarrhoea
- Inability to coordinate sucking, necessitating introduction of tube feeding
- Baby inconsolable after 2 consecutive feeds

**4.3. Differential diagnosis**

Opioid-related NAS may mimic other conditions. No clinical signs should be solely attributed to drug withdrawal without a careful assessment to exclude other causes. Therefore, it is important to rule out sepsis, hypoglycemia, hypocalcemia, hyperthyroidism, intracranial haemorrhage, hypoxic ischemic encephalopathy, and polycythaemia/ hyper viscosity syndrome.

**4.4. Timescale of withdrawal**

This will vary depending on type of drug taken, amount of drug taken, how recently drugs were taken, any use of multiple drugs simultaneously and maternal physiology.

**Table 1. Time of onset of symptoms**

Name of drug	Onset of symptoms	Comments	Recommended observation period*
<b>Heroin</b>	24 - 48 hours	Duration may be 8-10 day	5-7 days
<b>Cocaine</b>	24 - 48 hours	May be 48 – 72 hours	3-5 days
<b>Amphetamines</b>	24 hours	Duration 7- 10 days	3-5 days
<b>Methadone</b>	48 - 72 hours	Duration up to 30 days	5-7 days
<b>Buprenorphine</b>	36 – 60 hours	Duration up to 28 days	5-7 days
<b>Barbiturates</b>	4-7 days	Can be 1-14 days	5-7 days
<b>Benzodiazepines</b>		Can be >10 days	5-7 days
<b>SSRI &amp; TCA</b>	1-3 days	Duration 2 – 6 days	2-3 days
<b>Prescription opioid medications</b>	36 – 72 hours	Duration 10 – 30 days	3-5 days

**Table 2: Length of time during which urine will remain positive**

Name of drug	Length of time during which urine will be positive after last dose
<b>Heroin, Morphine, Codeine</b>	1-2 days
<b>Cocaine</b>	3-4 days – longer with heavy use
<b>Amphetamines</b>	1-2 days
<b>Methadone</b>	2-3 days
<b>Barbiturates: Short acting</b>	< 2 days
<b>Long acting</b>	1-7 days
<b>Benzodiazepines</b>	Up to 30 days
<b>Marijuana</b>	1-10 days – depending on amount



## 5. MANAGEMENT

Aims of managing a baby at risk of neonatal drug withdrawal are to:

- maintain normal body temperature
- reduce hyperactivity
- reduce excessive crying
- reduce motor instability
- ensure adequate weight gain and sleep pattern
- identify significant withdrawal requiring pharmacological treatment

### 5.1. Antenatal management

- Any pregnant woman identified as an ongoing user of recreational drugs (such as heroin, cocaine etc.), significant alcohol or significant doses of prescribed opiate or other relevant drugs will be informed that her baby will be electively admitted to neonatal unit and observation for 5 days or more will be needed.
- It is not possible to predict the development of NAS in individual babies, and so babies should not be discharged before the 5th day. Occasional use of cannabis, or single dose antidepressant use should not normally require 5 days' monitoring postnatally.
- During antenatal care, the obstetrician should assess the level of drug and/or alcohol consumption at 34 weeks, and following discussion with the mother, inform FPU and alert the pediatric team.
- Check maternal hepatitis B, hepatitis C and HIV status and decide on the management plan for the baby.

Make sure to know:

- Type, amount and duration of drug(s) exposure
- Route of administration
- When last dose was taken

### 5.2. At the time of delivery

- **Do not give naloxone** (can exacerbate withdrawal symptoms)
- Care of the baby should include encouragement of skin-to-skin contact depending on the mother's mental status/ability and initiation of early breastfeeding depending on the type, timing & duration of drug use.

### 5.3. Postnatal management

The following babies are considered at risk of neonatal abstinence syndrome and should be admitted to the neonatal unit after delivery.

- Ill babies
- Babies who are to be discharged into foster care
- Babies whose mothers are unable to remain in hospital with the baby
- Babies born < 33 weeks gestation
- Babies born < 1800g

All other NAS babies will be admitted to post-natal ward with their mothers.

- **To inform FPU in every case where mother is known to be suspected substance abuser**
- **To admit all babies who are considered at risk of NAS**

#### On admission

- On admission to NICU or post-natal ward, in addition to taking a careful general and drug history, check and record in baby notes
  - Results of Hepatitis C (relatively common in users), Hepatitis B (less common but preventable) and HIV (not common but very important)
  - Background social information, discuss with family protection unit (FPU) to facilitate discharge planning
  - Check for any antenatal plan for breastfeeding
  - Any other missing antenatal care/ investigations
- On admission examination, **check** for possible congenital anomalies (increased risk but still rare), and signs of other illnesses e.g. sepsis/ complications of possible IUGR.
- **Inform FPU and ensure to send the urine (preferably first urine sample) and blood** for toxicology and stored in an appropriate medium and temperature till it can be transported to the laboratory for analysis.

- **Pre- and postductal saturations** should be carried out within 24 hours of birth for all babies whose mothers have been on SSRI to detect persistent pulmonary hypertension of the newborn (PPHN).
- Consider performing a **cranial ultrasound scan** for all babies whose mothers have abused **cocaine**, particularly if heavy amounts of cocaine have been used.
- Routine Hepatitis B vaccine should be offered to both mother and baby if mother is Hepatitis B negative where narcotic abuse is identified.
- **Score regularly** to assess progress of any abstinence or response to treatment (see guideline flowchart below).
- Ensure postnatal baby check and **daily review by a paediatrician**.
- Observe in the hospital for **minimum 5 days**.
- Strict patient/family confidentiality must be maintained.

### Breastfeeding

- Strongly recommend breastfeeding unless contraindications exist or if the baby is going for adoption.
- A recommendation should be made to abstain from breastfeeding if a woman expresses an intent to continue substance use **and** refuses substance use treatment.
- Breastfeeding should be encouraged for babies born to mothers who used an illicit substance, such as opioids, PCP (phencyclidine) or cocaine, but discontinued and are on stable methadone or buprenorphine maintenance therapy) (CDC).

### Assessment

- Scoring should be initiated within 2 hours of life, and continued for minimum 5 days to assess for possible neonatal withdrawal symptoms and signs.
- For babies with minor signs, use non-pharmacological management.

### 5.3.1. Non-pharmacological interventions

**Table 3.**

#### **High pitched/excessive cry**

- Soothe the infant with swaddling, talk quietly, hold infant firmly to body, rock gently.
- Reduce environmental stimuli (slow movements, reduce lighting and noise level, cover head end of cot).

#### **Sleeplessness**

- Reduce environmental stimuli
- Swaddle infant, minimise handling, rock gently and encourage cuddles.

#### **Excoriation**

- Apply protective skin barriers to affected areas.

#### **Hyperthermia**

- Dress in light clothing and use lightweight, soft fabric to swaddle.
- Nurse in an open cot with adequate ventilation

#### **Nasal flaring/ Tachypnoea**

- Avoid swaddling so that respiratory rate can be closely observed.

#### **Excessive sucking of fists**

- Apply mittens, keep hands clean, and consult with parents about the use of a pacifier.

#### **Poor feeding**

- Feed to demand, offer small frequent feeds, and allow resting between sucking
- Reduce environmental stimuli during feeds and assess coordination of suck swallow reflex.
- Weigh and assess hydration daily to ensure infant achieve required fluid intake or know excessive weight loss.

#### **Vomiting**

- Wind/ Burp infant regularly when he/she stops sucking and at the end of the feed.

#### **Peri-anal excoriation**

- Due to Loose Stool/Diarrhoea
- Change infants' nappy with every feed
- Use of appropriate barrier creams, and it may be necessary to expose the buttocks to air to dry

### 5.3.2. Pharmacological treatment

- Pharmacological treatment is an important component of management when nonpharmacologic care is insufficient to mitigate signs and symptoms of the neonatal abstinence syndrome. Approximately 60 to 80% of infants with the syndrome do not have a response to nonpharmacologic treatment and require medication.
- Start pharmacological treatment (**after other causes excluded**) if there is:
  - **3 consecutive abstinence scores averaging > 8, or**
  - **≥ 12 for 2 consecutive scores**

**OR**

- **convulsions**
- **recurrent vomiting or profuse watery diarrhoea**
- **poor feeding requiring tube feeds**
- **inconsolability after 2 consecutive feeds**
- Once the score is 8 or higher the scoring intervals automatically become 2 hourly, so that significant symptoms are treated within 4-6 hours.
- If the score is 12 or higher the baby must be assessed by 2 medical professionals individually.
- When mother has been using an opiate or opioid, a morphine derivative is the most effective way to relieve symptoms.
- For NAS secondary to non-opiate drug use (including SSRI, SNRI, TCA, cocaine), phenobarbitone is considered first line treatment.
- When there has been multiple drug usage, phenobarbital may be more effective

#### *Common indications for adjunctive therapy*

1. poorly controlled withdrawal symptoms despite optimizing first line therapy,
2. inability to wean first line therapy, and
3. relapse after initial treatment.

### Morphine

- Start with 40 mcg/kg/dose oral 3-4 hourly, may be necessary to increase dose by 10 mcg/kg/dose increments
- If the baby is feeding well and settling between feeds, consider doubling the dose interval and, after 48 hr, reducing the dose by 10 mcg/kg/dose every 24-48 hr. If

major signs continue, discussed with experienced doctor/ consider need for other medication (e.g. phenobarbital) (see flow chart)

- ***Infants treated with an opioid should be on a cardiac and respiratory monitor, particularly in the initial period, to ensure there are no clinical signs of respiratory depression.***

\*\* If oral morphine is not available, IV morphine can be given with expert opinion.

### Phenobarbital

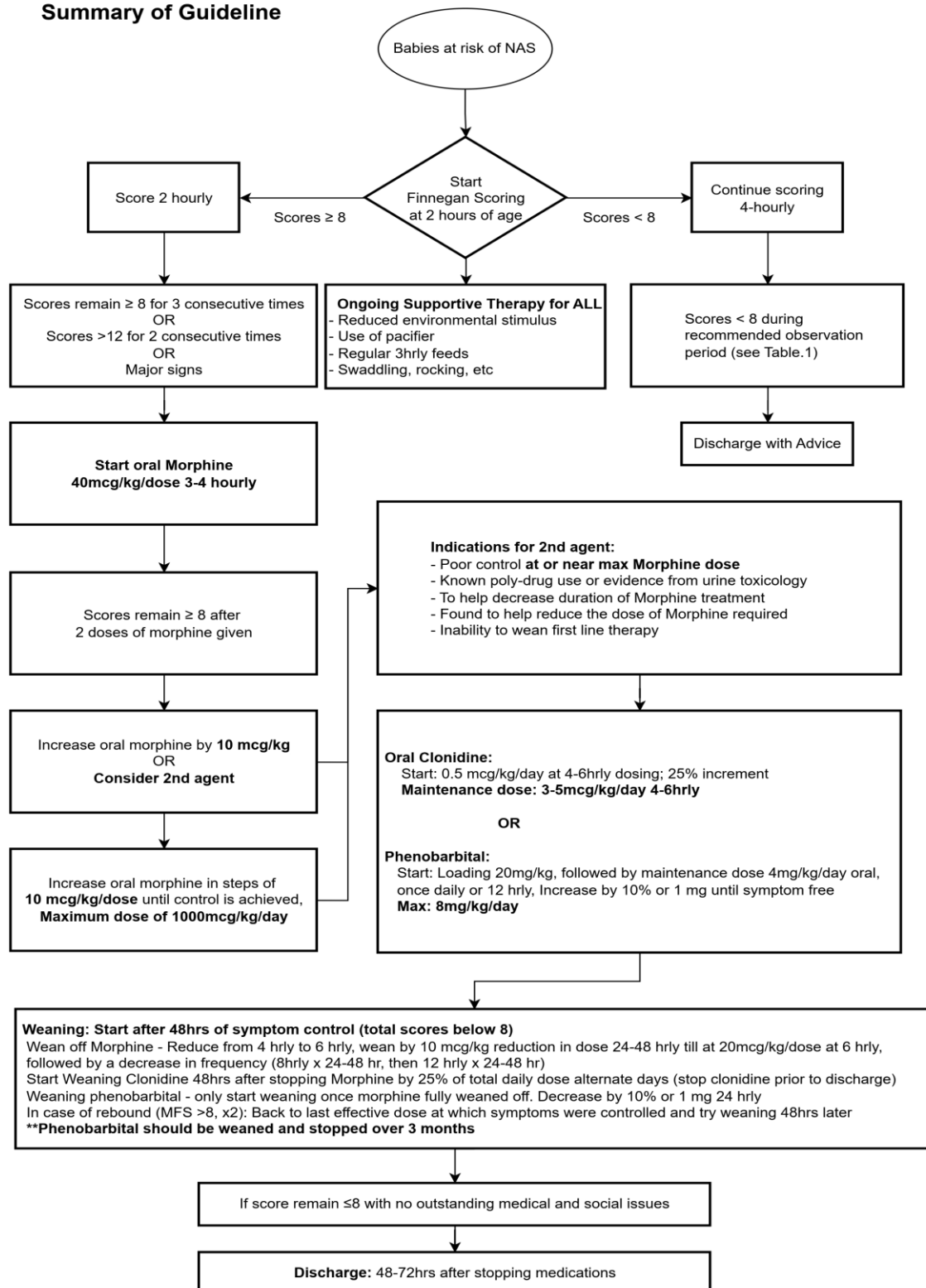
- For treatment of seizures and for babies of mothers who are dependent on other drugs in addition to opiates and suffering serious withdrawal symptoms, give loading dose of Phenobarbital 20 mg/kg IV over 20 min, then maintenance 4 mg/kg oral daily, in addition to morphine as above (see guideline flowchart below).
- If there are seizures then the infant should be admitted to the neonatal unit urgently and treated as per local seizure guideline.

### Chlorpromazine

- For babies of mothers who use benzodiazepines, give chlorpromazine 1 mg/kg oral 8 hrly if showing signs of withdrawal
- Dose can be doubled if withdrawal is severe. Maximum dose is 6 mg/kg/day.
- Once dose is stable, reduce dose by not more than 2mg/kg/day every 3rd day.
- Remember chlorpromazine can reduce seizure threshold

## 6. GUIDELINE FLOW CHART

### Summary of Guideline



Adapted from Neonatal guideline 2022-2024 by the Bedside Clinical Guidelines Partnership and West Midlands Neonatal Operational Delivery Network, NHS, Thames Valley and Wessex Neonatal Abstinence Syndrome Guideline, version Jan 3, 2023

## 7. DISCHARGE AND FOLLOW-UP

- Clinical signs of NAS may last for months, and infants with NAS are two-and-a-half times more likely to be readmitted to the hospital within 30 days of discharge, compared to uncomplicated term infants.

The following are criteria for discharge for infants who were medically treated for NAS:

- The infant should be clinically stable with good weight gain and adequate oral feeding.
- Co-morbidities have been treated or controlled so that outpatient care would be appropriate.
- The infant remains below treatment threshold after discontinuation of drug for at least 24 to 48 hours.
- If the infant is to be discharged on continued drug therapy (phenobarbital), NAS scores should be less than 8 for 48-72 hours and the home environment has been assessed for safety.

### 7.1. Discharge

Ensure discharge planning involving:

- FPU plan
- Caretaker and family support
- Assessment of the family and home environment has taken place.
- Alternate living arrangements have been made for the infant if the home environment has been determined to be unsafe.
- Follow up plan
- For babies who did not require treatment or if no signs of withdrawal, discharge after 5 days and arrange follow-up with pediatrician
- For babies who required treatment/ if seizures occurred, discharge after 48-72 hr after stopping medications. Arrange regular follow-up in high risk clinic with pediatrician after discharge.



## 7.2. Follow up

- For infants discharged on phenobarbital, it should be weaned gradually and aimed at stopping the medication within the first 3 months of age.
- Arrange regular pediatric consultant follow-up for all the symptomatic babies who required treatment.
- Follow up as per high-risk clinic protocol and neuro-development assessment should be done as per high-risk infant protocol.

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**APPENDICES**

**Table 4. Modified Finnegan Neonatal Abstinence Score sheet**

<b>Modified Finnegan Neonatal Abstinence Score Sheet</b>														
<b>System</b>	<b>Signs and Symptoms</b>	<b>Score</b>	<b>AM</b>					<b>PM</b>					<b>Comments</b>	
<b>Central Nervous System Disturbances</b>	Excessive high-pitched (or other) cry < 5 mins	2												
	Continuous high-pitched (or other) cry > 5 mins	3												
	Sleeps < 1 hour after feeding	3												
	Sleeps < 2 hours after feeding	2												
	Sleeps < 3 hours after feeding	1												
	Hyperactive Moro reflex	2												
	Markedly hyperactive Moro reflex	3												
	Mild tremors when disturbed	1												
	Moderate-severe tremors when disturbed	2												
	Mild tremors when undisturbed	3												
	Moderate-severe tremors when undisturbed	4												
	Increased muscle tone	1												
	Excoriation (chin, knees, elbow, toes, nose)	1												
	Myoclonic jerks (twitching/jerking of limbs)	3												
Generalized convulsions	5													

metabolic/ Vasomotor/ Respiratory Disturbances	Sweating	1																	
	Hyperthermia 37.2-38.3C	1																	
	Hyperthermia > 38.4C	2																	
	Frequent yawning (> 3-4 times/ scoring interval)	1																	
	Mottling	1																	
	Nasal stuffiness	1																	
	Sneezing (> 3-4 times/scoring interval)	1																	
	Nasal flaring	2																	
	Respiratory rate > 60/min	1																	
	Respiratory rate > 60/min with retractions	2																	
Gastrointestinal Disturbances	Excessive sucking	1																	
	Poor feeding (infrequent/uncoordinated suck)	2																	
	Regurgitation ( $\geq 2$ times during/post feeding)	2																	
	Projectile vomiting	3																	
	Loose stools (curds/seedy appearance)	2																	
	Watery stools (water ring on nappy around stool)	3																	
	<b>Total Score</b>																		
	<b>Date/Time</b>																		
	<b>Initials of Scorer</b>																		

Finnegan LP. Neonatal abstinence syndrome: assessment and pharmacotherapy. In: Nelson N, editor. Current therapy in neonatal-perinatal medicine. 2 ed. Ontario: BC Decker; 1990.

- The NAS score sheet lists 21 symptoms that are most frequently observed in opiate-exposed infants. Each symptom and its associated degree of severity are assigned a score and the total abstinence score is determined by totaling the score assigned to each symptom over the scoring period.

### Key points

- The first abstinence score should be recorded approximately two hours after birth or admission to the nursery (baseline score). This score reflects all infant behavior up to the first scoring interval time point.
- Following the baseline score all infants should be scored at 4-hourly intervals, except when high scores indicate more frequent scoring.
- The score sheet allows for 2-hourly scoring over the 24-hour period.
- A new sheet should be started at the beginning of each day.
- Scoring is dynamic. All signs and symptoms observed during the scoring interval are included in the point-total for that period.
- If the infant's score at any scoring interval is  $\geq 8$ , scoring is increased to 2-hourly and continued for 24 hours from the last total score of 8 or higher.
- If the 2-hourly score is  $\leq 7$  for 24 hours then 4-hourly scoring intervals may be resumed.
- If pharmacotherapy is not needed the infant is scored for the first 4 days of life at 4-hourly intervals.
- If pharmacotherapy is required the infant is scored at 2- or 4-hourly intervals, depending on whether the abstinence score is less than or greater than 8 throughout the duration of therapeutic period.
- If after cessation of pharmacotherapy the score is less than 8 for the following 3 days, then scoring may be discontinued.
- If after cessation of pharmacotherapy the score is consistently 8 or more, then scoring should be continued for the following 4 days (minimum) to ensure that the infant is not likely to develop late onset of withdrawal symptoms at home following discharge.

### Guide to assessment and scoring

- The neonatal abstinence syndrome scoring system was designed for term babies on four-hourly feeds and may therefore need modification for preterm infants. In a term infant scoring should be performed 30 minutes to one hour after a feed, before the baby falls asleep.
- If necessary, the infant should be awakened to elicit reflexes and behavior, but if the infant

is woken to be scored then diminished sleep after scoring should not be recorded. A crying infant should be soothed and quietened before assessing muscle tone, Moro reflex and respiratory rate.

**Morphine Dosing of the Vomiting Infant**

- Ensure that the infant is not being overfed and that the infant is being appropriately postured during and after feeding. Give the morphine dose 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 infant vomits after feeding, do not give further morphine (always err on side of caution).

High-pitched cry	Score 2 if high-pitched at its peak, 3 if high-pitched throughout. Infant is scored if crying is prolonged, even if it is not high-pitched. <sup>2</sup>
Sleep	This is a scale of increasing severity and a term infant should receive only one score from the three levels of severity. A premature infant on 3 hourly feeds can sleep for 2½ hours at most. Scoring should thus be 1 if the baby sleeps less than 2 hours, 2 if less than 1 hour and 3 if the baby does not sleep between feeds. <sup>2</sup>
Moro reflex	The Moro or startle reflex is a normal reflex of young infants and occurs when a sudden loud noise causes the child to stretch out the arms and flex the legs. Score if the infant exhibits pronounced jitteriness (rhythmic tremors that are symmetrical and involuntary) of the hands during or at the end of a Moro reflex. Score 3 if jitteriness and clonus (repetitive involuntary jerks) of the hands and/or arms are present during or after the initiation of the reflex.

Tremors	This is a scale of increasing severity and an infant should only receive one score from the four levels of severity. Undisturbed refers to the baby being asleep or at rest in the cot.
Increased muscle tone	Score if excessive or above-normal muscle tone or tension is observed - muscles become "stiff" or rigid and the infant shows marked resistance to passive movements, e.g. if the infant does not experience any head lag when being pulled to the sitting position; or if there is tight flexion of the infant's arms and legs (unable to slightly extend these when an attempt is made to extend and release the supine infant's arms and legs).
Excoriation	Excoriations (skin abrasions resulting from constant rubbing against a surface that is covered with fabric such as bed linen). Score only when excoriations first appear, increase or appear in a new area.
Myoclonic jerks	Score if involuntary muscular contractions which are irregular and exceedingly abrupt (usually involving a single group of muscles) are observed.
Generalized convulsions	In the newborn infant generalized seizures or convulsions are often referred to as tonic seizures. They are most commonly seen as generalized activity involving tonic extensions of all limbs, but are sometimes limited to one or both limbs on one side. Unusual limb movements may accompany a seizure. In the upper limbs these often resemble "swimming" or "rowing". In the lower limbs, they resemble "pedaling" or "bicycling." Other subtle signs may include eye staring, rapid involuntary movements of the eyes, chewing, back arching, and fist clenching.
Sweating	Score if sweating is spontaneous and is not due to excessive clothing or high room temperature
Hyperthermia	Temperature should be taken per axilla. Mild pyrexia (37.2-38.3°C) is an early indication of heat produced by increased muscle tone and tremors.
Yawning	Score if more than 3 yawns observed within the scoring interval.
Mottling	Score if mottling (marbled appearance of pink and pale or white areas) is present on the infant's chest, trunk, arms, or legs.
Nasal stuffiness	Score if the infant sounds congested; mucous may be visible.
Sneezing	Score if more than 3 sneezes observed within the scoring interval.
Nasal flaring	Score only if repeated dilation of the nostrils is observed without other ev-

	idence of lung or airways disease.
Respiratory rate	Respirations are counted for one full minute. Score only if >60 per minute without other evidence of lung or airways disease. Score 2 if respiration involves drawing in of the intercostal muscles (retractions).
Excessive sucking	Score if hyperactive/disorganized sucking, increased rooting reflex, or attempts to suck fists or thumbs (more than that of an average hungry infant) are observed.
Poor feeding	Score if the infant demonstrates excessive sucking prior to feeding yet sucks infrequently during a feeding taking a small amount of breast milk or formula, and / or demonstrates an uncoordinated sucking reflex (difficulty sucking and swallowing). Premature infants may require tube feeding and should not be scored for poor feeding if tube feeding is expected at their gestation.
Regurgitation	Score if at least one episode of regurgitation is observed even if vomit is contained in the mouth.
Loose/watery stools	Score if loose (curds/seedy appearance) or watery stools (water ring on nappy around stool) are observed. Check the nappy after the examination is completed if not apparent during the examination.



