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Working with Pain in Labour:

Systemic Medications

- **Morphine**
- **Hydromorphone**
- **Fentanyl**
- **Nitrous oxide**

July 2019

This document is intended as a resource to guide health professionals' practice in the labour and birth setting only.

Practices may differ across facilities, depending on available resources and prescriber preference. All policies and procedures must be approved by the appropriate processes within each facility/Nova Scotia Health Authority (i.e.: Maternal/Child or Perinatal Committee, Medical Advisory Committee, etc.).

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INTRODUCTION: UNDERSTANDING PAIN DURING CHILDBIRTH

Pain is a subjective and complex phenomenon, and its role in childbirth is physiologic. Pain sensations in labour trigger the production of endogenous hormones (e.g. endorphins and oxytocin) which provide comfort and enhance a sense of calm. Adequate preparation to promote self-confidence and skilled support are key resources to assist the childbearing person to work with the pain of labour, and to enable them to achieve a healthy birth.

Marchand et al (2015) describe four dimensions of pain:

1. Nociceptive (noxious stimuli)
2. Sensory-discriminative (intensity)
3. Affective-motivational (unpleasant, emotional)
4. Cognitive-behavioural (behaviour)

Labour pain will be experienced and expressed differently by each individual, and can include any or all of these dimensions. The contribution of each dimension of pain throughout labour is described here:

Pain Dimension	How it Contributes…	Consideration for Intrapartum Care Provider
Nociceptive	Perception of real or potential injury related to stretching of tissues: • 1st stage of labour: cervix, ligaments, muscles, adjacent tissues • 2nd stage of labour: traction and stretching of pelvic floor, perineum, perineal muscles, pelvic cavity, and roots of sacral nerves. Influenced by fetal position	Encourage women to ambulate and move freely into more comfortable positions. Avoid interventions that restrict mobility.
Sensory-discriminative	Perception of intensity and threshold of pain	Modulate perception: • **Gate Control Theory** e.g. ambulation, gentle massage, stroking, hydrotherapy, vibrations • **Diffuse Noxious Inhibitory Control (DNIC)** e.g. acupressure, sterile H_2O injections, deep massage • **Pharmacological approaches** e.g. opioids, N_2O, regional analgesia/anaesthesia

Pain Dimension	How it Contributes…	Consideration for Intrapartum Care Provider
Affective-motivational	Gauges the unpleasantness of pain; affected by emotions, values, and experience Differentiates 'Pain' from 'Suffering'	Employ measures that engage higher centres of the brain: • Emotional support • Comfort measures • Provide information/advice • Advocacy • Supporting the partner *these measures extend beyond this pain dimension to enhance other examples in this table
Cognitive-behavioural	Personal expression of the pain experience, influenced by these factors: • Cultural • Emotional • Motivational • Social • Cognitive	Early in care encounter: Focus on building relationship with labouring patient, exploring hopes, fears, and expectations for birth experience and wishes for analgesia. Throughout care encounter (e.g.): • 'checking in' between contractions for verbal confirmation of coping • ongoing assessment of muscle tension and breathing • 'taking charge' if panic or despair are present; convey reassurance, confidence and calmness until patient regains inner strength

Central to the role of the intrapartum care provider is early establishment of a relationship with the labouring person. Drawing from a repertoire of assessment skills and supportive measures, the intrapartum care provider optimizes the patient's ability to work with the pain of labour and to avoid suffering.

Suffering occurs in labour when the experience and perception of pain exceed the person's capacity for coping, or the person is unable to activate the mechanisms for coping (SOGC 2018). The most effective way to prevent suffering is to address the emotional component of pain (i.e. utilizing support and non-pharmacological approaches). All comfort

measures, however, should be consistent with the wishes of the labouring person, who is encouraged to express their needs early in the care encounter and as labour progresses. Parenteral opioids and nitrous oxide (N_2O) are commonly requested.

Informed Decision-Making:

Information about pain management options for labour and birth should be reviewed as part of routine prenatal care. This information should include indications for, as well as risks and benefits of pain management options available during labour: discuss associated maternal and neonatal side effects, the potential effect on labour progression and the establishment of breastfeeding. Individual preferences and concerns should be addressed and taken into consideration, and informed (verbal) consent must be obtained and documented. Antenatal consultation with an anaesthesiologist should be arranged when indicated.

Pharmacological Options – Opioids for Labour Pain

There are **typically three parenteral medication choices for labour analgesia** used in Nova Scotia hospitals. All are opioids: **morphine, HYDROmorphone,** and **fentaNYL,** which are preferentially given intravenously or subcutaneously. Intramuscular injection, while a recognized route of administration, is considered to be unnecessarily painful and is discouraged. The choice of any of these options depends on the stage of labour, patient preference, and the preference of the ordering physician or midwife. A 2018 Cochrane review reports that it is unclear how effective opioids are for labour pain management, which opioid is best, and how adverse effects can be avoided. For labouring patients who choose opioids, a summary usage table is provided in Appendix A.

The choice of a parenteral opioid assists the labouring patient to address only one dimension of labour pain (sensory-discriminative), but it does not remove pain entirely.

A patient's decision to choose opioids in labour does not diminish or eliminate the need for intrapartum care providers to continue their supportive/assistive role.

Potential side effects associated with intrapartum opioid use include:	
Maternal	Nausea, vomiting, dysphoria, impaired ability to engage in decision-making about care; delayed gastric emptying, respiratory depression and desaturation, allergic or hypersensitivity reaction including anaphylaxis.
Fetus/newborn	Decreased fetal heart rate and/or variability, respiratory depression, desaturation up to 12 hours of age, possible interference with cuing and feeding efforts. *Newborn side effects depend on the dose and timing of maternal opioid administration*.
Side effects are dose-related and specific to the opioid selected; health professionals should aim to provide the lowest dose possible to achieve the desired degree of pain relief.	

Stage of Labour and Choice of Opioid:

A physician's order is required before opioid can be administered.

Opioids with longer duration of action are better suited for use in the latent phase or early active stage of labour, in order to reduce the risk for newborn respiratory depression. Women receiving IV opioids or regional anaesthesia during active labour (as determined by cervical change and contraction pattern) must have a vaginal examination performed within 30 minutes prior to receipt, with the findings documented.

- **Morphine**

Drug information: Morphine is a naturally occurring substance that was first isolated in the 1800's from the opium poppy; it has been used in obstetrics since the early 20th century. Its duration of effect is 3-4 hours, with a half-life of 1 hour for maternal use and a half-life of 6 hours in neonates. It has no active metabolites and so most infants delivered $\geq$ 3 hours after maternal administration have no detectable cord levels. Morphine, however, is more sedating and has a longer half-life than fentaNYL, making it a better choice for latent or early active labour.

- **HYDROmorphone (e.g. Dilaudid)**

Drug information: Although it has a drug profile comparable to that of morphine, HYDROmorphone is 5 times more potent than morphine when comparing mg to mg. Health professionals must be mindful of these differences when ordering and administering HYDROmorphone, particularly for patients who are opioid-naive.

FentaNYL

Drug information: FentaNYL is a lipid-soluble synthetic opioid with an analgesic potency 75-100 times greater than morphine. Additionally, fentaNYL lacks active metabolites and produces potentially fewer and less severe maternal side effects than morphine. When administered intravenously it has an almost immediate onset of action (peak effect 5-10 minutes) with a relatively short duration of action of 30-60 minutes, a maternal half-life (T ½) of < 1 hour and a neonatal T ½ of 1-6 hours. These combined properties make fentaNYL a suitable option for pain management in active labour, although users should exercise caution if birth is imminent.

Additional considerations: Intravenous (IV) opioid administration is not without risk, and is dose-related (see table of side effects above).

Because of the potential for adverse effects Registered Nurses (RNs), midwives, or physicians must demonstrate competency in safe administration of IV opioids, and fentaNYL in particular. Demonstration of initial and ongoing competency regarding intrapartum IV fentaNYL administration is a facility-specific responsibility, but should include education, practice supports such as local clinical policy, and confirmation by locally acknowledged content and/or practice experts.

RNs who administer IV fentaNYL must also have current Provider status for Cardio-Pulmonary Resuscitation and Neonatal Resuscitation (CPR and NRP).

SPECIAL CONSIDERATIONS WHEN USING FENTANYL

Contraindications to use of FentaNYL:

- ❑ Allergy to fentaNYL
- ❑ Uncorrected hypotension or hypovolemia
- ❑ Liver or kidney disease
- ❑ Significant respiratory compromise (e.g. severe asthma, cystic fibrosis, COPD, obstructive sleep apnea, etc.)
- ❑ Concurrent use of monoamine oxidase inhibitors (MAOI) or MAOI use within the previous two weeks
- ❑ Presence of fetal acidosis
- ❑ Maternal respiratory rate less than 8/minute, or O_2 saturation less than 94%
- ❑ Inability to provide 1:1 intrapartum care
- ❑ Somnolence score greater than 2

Use with Caution:

- ❑ Preterm labour (increased risk of respiratory depression in the neonate)
- ❑ Obesity: BMI greater than 45 (increased risk of airway complications and of undiagnosed sleep apnea)
- ❑ Women who have received other opioids (depending on the duration of action), or repeated doses of fentaNYL.
- ❑ Within ½ hour of anticipated delivery
- ❑ Concomitant use of antipsychotics
- ❑ Women at high risk for emergency cesarean delivery (e.g. evidence of fetal compromise, multiple fetuses)
- ❑ Women with a history of difficult intubation
- ❑ Presence of hypertensive disease of pregnancy (end-organ involvement increases sensitivity to hemodynamic effects of fentaNYL)
- ❑ Allergy or hypersensitivity reaction to other narcotics as cross reactions may occur

Administration:

Subcutaneous (SubQ) and intramuscular (IM) routes of administration involve painful injections, delay in onset, and variable absorption leading to unpredictable plasma levels. Because fentaNYL has a short half-life, multiple doses may be required and so it is recommended that fentaNYL be given by the direct IV route. IV administration has a faster onset with less variability of peak concentrations, and enables more effective titration of dosing. Methods of IV administration include direct intermittent boluses provided by the RN, midwife, or physician; or via patient controlled analgesia (PCA) method.

FentaNYL should NOT be administered by continuous infusion as this may deliver more medication than is required, with a subsequent increase in side effects and no improvement in therapeutic effect as compared to intermittent direct IV administration.

Administer using slow IV push method (rapid IV infusion may result in skeletal muscle and chest wall rigidity, impaired ventilation, respiratory distress, apnea or bronchoconstriction).

Neither initial nor subsequent doses of fentaNYL should be administered when any of the following signs are present:

- ***respiratory rate less than 8 breaths per minute***
- ***oxygen saturation less than 94%***
- ****Somnolence Score* greater than 2***
  - ***1*** *= awake and alert: no action needed*
  - ***2*** *= sedated but arousable: no action needed*
  - ***3*** *= heavily sedated and difficult to arouse, drifts off during conversation:* ***requires action/decrease dose***
  - ***4*** *= unresponsive or somnolent, minimal or no response to physical stimulation:* ***unacceptable, stop opioid, consider administering Naloxone***

Dosing:

- **Initial dose:** 50 micrograms slow IV direct (i.e. over 1 to 3 minutes) x 1 dose.
- **Wait 10 minutes for effect and assess for subsequent dose(s).** Repeat 50 micrograms slow IV direct every 10 minutes as needed until adequate analgesia is achieved, or maximum hourly dosage is reached.
- **Maximum hourly dose: 300 micrograms**
- If satisfactory pain relief is not achieved despite administration within these dose limits, anaesthesia should be consulted and consideration given to alternative pharmacological or regional methods of pain management (e.g. epidural analgesia or IV PCA fentaNYL).

Assessment and Monitoring:

- **Prior to any fentaNYL administration**, assess and record blood pressure, pulse, respirations, oxygen saturation, fetal heart rate, pain scale and somnolence score (see above).
- **Following fentaNYL administration:** continuous patient monitoring is required during fentaNYL administration and up to 1 hour post, provided patient somnolence score is less than or equal to 2.

- **Blood pressure, pulse, and respiration:** assess and record 15 minutes after administration and then q1h x 4 hours.
- **Maternal oxygen saturation (SpO_2):** All women receiving IV fentaNYL should have their SpO_2 CONTINUOUSLY monitored for one hour following the last dose of fentaNYL. This should be recorded at the same frequency as other maternal vital signs.
- **Fetal heart rate:** assess and record as per SOGC guideline for intrapartum fetal surveillance (2007). Opioids commonly reduce fetal heart rate (when using intermittent auscultation) and can also cause a decrease in the baseline and variability (if using continuous electronic fetal monitoring).
- **Pain/coping and somnolence score:** assess and record every 30 minutes

Patient controlled analgesia (PCA): *per UpToDate 2019*:

"Use of a PCA pump allows the patient to intravenously self-administer a programmed dose of medication with minimum intervals between doses. Although the analgesic efficacy of intravenous PCA does not match that of neuraxial (epidural, spinal, or combined spinal/epidural) analgesia, this method of opioid administration is the most effective option for the parturient in whom neuraxial analgesia is contraindicated, not desired, or not available. PCA provides rapid onset of analgesia, better control of pain relative to side effects than parenteral opioid injection, and a sense of control for the patient. In general, shorter-acting opioids are preferred in the labor setting to allow rapid changes in plasma levels to match the changing clinical need."

The availability of PCA for labour pain varies across facilities in Nova Scotia.

MANAGEMENT OF ADVERSE REACTION

If ANY of the following signs of adverse reaction occur:

- ❑ respiratory rate less than 8 breaths per minute
- ❑ oxygen saturation less than 94%
- ❑ somnolence score greater than 2

- ✓ Immediately stop the injection and do **NOT** repeat fentaNYL administration
- ✓ Notify responsible physician or anaesthesia
- ✓ Give oxygen by non-rebreather mask at 8-10 litres/minute and begin or continue oxygen saturation monitoring
- ✓ Ensure Naloxone 0.4mg IV is available
- ✓ **If patient is unresponsive, call Code Blue**

Treating Opioid-Induced Respiratory or Neurobehavioural Depression

The narcotic antagonist, naloxone hydrochloride (Narcan®), is a specific antidote against respiratory or neurobehavioural depression, which may result from overdosage or unusual sensitivity to opioids. Therefore, if clinical signs indicate respiratory depression an appropriate dose of this antagonist should be administered simultaneously with ventilatory support. Specifically, patients who have received fentaNYL are more susceptible to such effects due to its potency. As the duration of action of naloxone is shorter (20-60 minutes) than some opioids, it may need to be repeated in 3-5 minutes depending on patient response.

Adult Dosing Guidelines for Naloxone

Adult: 0.4-2 mg/dose IV every 2-3 minutes as needed. Use 0.1-0.2 mg IV every 2-3 minutes as needed for opioid-dependent patients

Lower doses may be effective without eliminating the therapeutic effect of fentaNYL; however, respiratory depression is a medical emergency. If there is no response after 10 mg, diagnosis of opiate toxicity should be questioned.
Depending on the dose and timing of maternal fentaNYL administration, the duration of action may exceed that of Naloxone; therefore, repeat doses may be needed.

- Preferred route is IV (quickest onset of action), but may also be given IM, ET, or SC.
- Onset of action may be delayed when given IM if patient has poor perfusion.
- Abrupt reversal of narcotic depression may result in symptoms of withdrawal in opioid-dependent patients.

Naloxone (Narcan®) Administration and Newborns

Neonates born to mothers who received opioid analgesia within four hours prior to delivery are at higher risk for respiratory depression. Those responsible for newborn care during the immediate period of transition to extrauterine life (usually Birth Unit RNs) must provide careful ongoing assessment and nursing care per unit routine for the first few hours after birth to ensure problems with transition are recognized, and appropriate interventions are initiated. The rapid newborn assessment tool, the “RAPPT” (respiratory, activity, perfusion, position, and tone), is a way to evaluate an infant’s physiologic condition and position during skin-to-skin contact and is a part of the newborn’s initial and ongoing assessment.

Historically, naloxone was commonly administered to newborns of mothers who had received opioids in labour. As of 2016, the textbook of Neonatal Resuscitation no longer supports this practice as there is insufficient evidence to evaluate the safety and efficacy of naloxone use in newborns. Animal studies and case reports have raised concerns about complications from naloxone, including pulmonary edema, cardiac arrest, and seizures.

Because the risk of neonatal respiratory depression and desaturation increases with larger doses of fentaNYL, oxygen saturation monitoring may be considered for at least 2 hours (longer – up to 8 hours - if there is an episode of desaturation) after birth for newborns whose mothers have received more than 250 micrograms. Neonates experiencing hypothermia may not show signs of respiratory depression as readily.

Short-term opioid exposure: For babies thought to be experiencing respiratory depression due to intrapartum opioid exposure, the Neonatal Resuscitation Program recommends providing support via positive-pressure ventilation as required. Insertion of an endotracheal tube or laryngeal mask for ongoing respiratory support may be required for newborns with prolonged apnea.

Longer-term opioid exposure: Infants of mothers receiving long-term narcotics, methadone or who are suspected of narcotic overuse should have appropriate respiratory support and monitoring, which includes ongoing screening for symptoms of withdrawal. Naloxone in this setting causes acute withdrawal and may lead to neonatal seizures.

Patient Monitoring after IV Naloxone Administration:
Adult: assess to ensure respiratory rate is greater than 8/minute. Consult an anaesthesiologist or the most responsible intrapartum care provider (MD or midwife) for recommendations regarding ongoing care.

Newborns: Naloxone is not recommended for use in neonates.

Inhaled Nitrous Oxide (N_2O)

Drug information: Nitrous oxide (N_2O) is an established option for pharmacological pain management in all stages of labour. The gaseous mixture used in obstetrical practice is 50% nitrous oxide and 50% oxygen; at this ratio N_2O has analgesic properties (higher concentrations of N_2O are considered mild anaesthetics). The mechanism of action is not fully understood, but it is thought to adhere to proteins within the neuronal membranes, altering ion flow through the membranes and affecting synaptic transmission.

Although it is not associated with complete pain control, N_2O is a viable, inexpensive, easily administered analgesic with varying patient reports of efficacy. Anxiolysis and endogenous opioid release are additional benefits of N_2O use. It may be used in conjunction with other methods of labour analgesia, both pharmacological and non-pharmacological.

N_2O has a very rapid onset; within 2 to 3 inhalations the patient will begin to feel the effect. It is also eliminated quickly through the lungs within a few breaths.

Additional considerations: N_2O is supplied in tanks or via a wall-installed system, and is inhaled and exhaled using a specially-designed mask or mouthpiece. This equipment incorporates a demand valve which ensures the gas is delivered only upon inhalation. Safety concerns related to women, fetuses, and members of the health-care team have been explored; however, the safety of its short-term use has been documented. Long-term implications are less known. N_2O exposure levels are expected to fall below recommended guidelines when the following measures are in place:

- Appropriate staff training to ensure compliance with equipment setup, including the use of scavenging devices in accordance with workplace safety standards.
- Labouring patients are instructed in self-administration and supported to experience optimal effects by being advised to begin breathing in and out fairly rapidly using the mask or mouthpiece at the earliest onset of uterine contractions (attending RN palpating for onset).
- Family members/support people attending the labour must be advised that N_2O must be self-administered, and that they cannot assist by holding the mask or mouthpiece.
- Appropriate staff training which highlights vigilance to ensure patient and their supports comply with the requirement for self-administration

An alternative to opioids, N_2O can also be used to promote comfort during other procedures associated with childbirth such as external cephalic version; placement of intravenous lines or balloons/Foley catheters for mechanical cervical ripening; manual removal of placenta; and laceration repair.

Benefits/Advantages to use of inhaled Nitrous Oxide:

- Non-invasive, low cost
- Retained mobility; bedrest is not required although vigilance for safety (falls risk) is recommended
- IV access is not required
- Very rapid onset and elimination
- Viable option to promote comfort during procedures when regional anaesthesia is not in use (e.g. external cephalic version, manual removal of placenta, perineal repair)
- No adverse effect on uterine activity
- May be used at any stage of labour
- Self-controlled administration, which contributes to satisfaction with the birth experience
- Substantial anxiolysis
- Lacks flammability
- Benign toxicity
- Not malodorous
- Causes minimal cardiac depression
- Does not trigger malignant hyperthermia
- Little to no neonatal effects

Risks/Disadvantages to use of inhaled Nitrous Oxide:

- Variable efficacy
- A small percentage of users may experience side effects during use, including nausea and vertigo. Again, vigilance for safety (falls risk) is recommended

Contraindications to use of inhaled Nitrous Oxide:

- Conditions that may create space for the collection of gas (e.g. recent pneumothorax, gastric bypass surgery, and inner ear surgery)
- Known significant B12 deficiency (because of the relationship between N2O and cobalamin binding)
- Pernicious anemia
- Impaired consciousness, whether by injury, medication, or drug or alcohol use (because this may adversely affect appropriate use of the equipment)
- Functional impairment that limits the use of the extremities
- Relative contraindications: methionine synthetase deficiency or reduction

Summary*:* Systemic Medication Use in Labour

1. **Intrapartum care providers must understand the dimensions of pain in labour, and draw from their repertoire of assessment skills and supportive measures to optimize the patient's ability to work with the pain and avoid suffering.**
2. **Health care providers should discuss pain management options for labour and birth as part of routine prenatal and intrapartum care. The discussion should include complete information on potential maternal and neonatal side effects in order for patients to make informed decisions about pain management.**
3. **Patients who choose systemic medications for labour pain continue to require skilled supportive care from trained intrapartum care providers.**
4. **Health care providers should consider a subcutaneous or IV route of administration for opioids (where multiple doses will be provided) to minimize tissue trauma, discomfort for the patient and enhance absorbability.**
5. **Health care facilities throughout Nova Scotia must have naloxone (opioid antagonist) readily available for administration if maternal respiratory depression occurs due to opioid administration for labour analgesia.**
6. **Naloxone is not recommended for use in neonatal resuscitation.**
7. **Neonates whose mothers received opioid analgesia within four hours of delivery, should be observed for respiratory depression for the first few hours post-delivery.**
8. **It is important to remember that neonates who are not adequately warmed may not show the signs of respiratory depression as readily.**
9. **Nitrous Oxide is a safe, established option for pharmacological pain management in all stages of labour. Its safety is enhanced by appropriately trained care providers, who instruct patients and their labour support people of its use.**

Recommendations: Parenteral Medication for Labour Analgesia *(July 2019)*

* Narcotics are known to cause respiratory depression; use with caution, and assess. Rev. 07/2019 with thanks to IWK Health Centre pharmacy and Dr. R. George

Medication	Route of Administration	Dosage	Onset of Action (minutes)	Expected Time to Maximum Analgesia (minutes)	Duration of Action
Morphine (latent phase or early active labour)	IV (slow push)	2-5 mg (IV) q2-4h prn	5 min.	**IV**: 20 min.	1-3 hours
	Subcutaneous (subQ)	10-20 mg (subQ) q3h prn	30-40 min.	**subQ**: 50-90 min.	2-6 hours
FentaNYL (early/late active labour & second stage labour) **Requires ongoing VS/SpO_2 assessment and monitoring (see pages 7 & 8)*	IV (slow direct: i.e. over 1 – 3 minutes)	**Initial dose**: 50 micrograms **Subsequent dose(s)**: 10 minutes following initial dose, give 50 micrograms slow IV direct every 10 minutes as needed until adequate analgesia is achieved or maximum hourly dosage is reached **Maximum hourly dosage** = 300 micrograms	Almost immediate	5-10 min.	30-60 minutes
	IV PCA	10-25 microgram bolus, 5-10 minute lockout, no background			
HYDROmorphone (latent phase or early active labour)	SubQ (although IM route may also be considered, it is unnecessarily painful and so SubQ is preferred)	0.8-2 mg q3h prn	15 min.	30-90 min	2-4 hours
	IV (slow push)	0.2-0.6 mg q2-4h prn	5 min.	Similar to Morphine profile	
	IV PCA	0.1-0.2 mg bolus with lockout of 6 minutes			
Opioid antagonist: Naloxone	IV	**Adults**: 0.4-2 mg IV q2-3 min. prn (doses as low as 0.04 mg may be effective for adults, depending on degree of sedation)	2 min.	n/a	20-60 minutes

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