Pharmacologic management of pain during labor and delivery

 INTRODUCTION — The way pain is experienced is a reflection of the individual's emotional, motivational, cognitive, social, and cultural circumstances [1]. The pain of childbirth is likely to be the most severe pain that a woman experiences during her lifetime [2]. Many women, especially nulliparas, rate the pain of labor as very severe or intolerable [3,4]. The pain of labor and delivery varies among women, and each labor of an individual woman may be quite different. As an example, an abnormal fetal presentation (eg, occiput posterior) is associated with more severe pain and may be present in one pregnancy, but not the next.

Pharmacological treatment of labor pain was introduced in the mid-nineteenth century. These analgesic techniques were controversial, as many women and their physicians strongly believed that labor pain was a natural and necessary accompaniment of childbirth. This battle continues to the present day, with a vocal minority arguing that the use of pharmacological analgesic agents in parturients is unnecessary, unnatural, and harmful. Thus, laboring women are often treated differently than other patients suffering from pain. The American College of Obstetricians and Gynecologists (ACOG) has recognized this double-standard, noting that there is no other circumstance in which it is considered acceptable to experience severe pain, amenable to safe relief, while under a physician's care [5,6]. ACOG supports the concept that maternal request alone is a sufficient medical indication for labor analgesia.

Although lower levels of labor pain have been correlated with higher levels of childbirth satisfaction, higher levels of labor pain do not preclude an overall satisfying experience. When interviewed after delivery, mothers tend to downplay the intensity of their labor pain [7] and it is not the most important factor influencing satisfaction with the childbirth experience [8]. However, a sense of personal control over decision-making processes in labor has consistently been shown to correlate with overall maternal satisfaction with childbirth. As an example, a study of 60 women who delivered vaginally found that personal control predicted greater maternal satisfaction [9]. Another study of 100 women undergoing vaginal delivery reported that satisfaction with pain relief was associated with a feeling of being in control and having input in the decision making process [10].

These findings suggest that women should be involved in the decision-making process regarding all aspects of childbirth, including pain relief, to increase maternal satisfaction.
This can be accomplished by educating women about pain relief techniques during pregnancy, prior to the onset of labor, so that women can carefully contemplate their options before labor commences, as rational decision-making is difficult during times of emotional stress and physical anguish. Furthermore, patient-controlled epidural analgesia (PCEA) empowers the parturient by giving her direct control of her pain relief, and this has the potential to increase maternal satisfaction [11-13].

Issues related to labor pain and pharmacologic modalities for pain relief will be reviewed here. Specific issues regarding administration and complications of neuraxial anesthesia and nonpharmacologic approaches to manage labor pain are discussed separately. (See "Neuraxial analgesia and anesthesia for labor and delivery: Options" and "Adverse effects of neuraxial analgesia and anesthesia for obstetrics" and "Nonpharmacological approaches to management of labor pain".)

**PAIN PATHWAYS** — Pain originates from different sites as the process of labor and delivery progresses.

**First stage of labor** — Pain at this time occurs during contractions, is visceral or cramp-like in nature, originates in the uterus and cervix, and is produced by distention of uterine and cervical mechanoreceptors and by ischemia of uterine and cervical tissues. The pain signal enters the spinal cord after traversing the T10, T11, T12, and L1 white rami communicantes. In addition to the uterus, labor pain can be referred to the abdominal wall, lumbosacral region, iliac crests, gluteal areas, and thighs.

Transition refers to the shift from the late first stage (7 to 10 cm cervical dilation) to the second stage of labor. Transition is associated with greater nociceptive input as the parturient begins to experience somatic pain from vaginal distention.

**Second stage of labor** — Somatic pain from distention of the vagina, perineum, and pelvic floor and stretching of the pelvic ligaments is the hallmark of the second stage of labor. The pain signal is transmitted to the spinal cord via three sacral nerves (S2, S3, and S4), which comprise the pudendal nerve. Second stage pain is more severe than first stage pain and is characterized by a combination of visceral pain from uterine contractions and cervical stretching and somatic pain from distention of vaginal and perineal tissues. In addition, the parturient experiences rectal pressure and an urge to "bear down" and expel the fetus as the presenting part descends into the pelvic outlet.

**ADVERSE CONSEQUENCES OF LABOR PAIN** — The pain of labor produces physiological changes in addition to emotional distress and suffering (table 1). These changes have an impact on many maternal systems, and also affect the fetus [14].

**Hyperventilation** — Hyperventilation consistently accompanies labor pain. Arterial CO2 partial pressures less than 20 mmHg are not uncommon, and profound hypocarbia may inhibit ventilatory drive between contractions and result in maternal hypoxemia, lightheadedness, and loss of consciousness [15]. Respiratory alkalosis, which impairs oxygen transfer from the maternal to fetal circulation, may occur. Alkalosis shifts the oxyhemoglobin dissociation curve to the left, increasing the affinity of oxygen for maternal hemoglobin, thereby decreasing off-loading of oxygen to the fetus. Maternal alkalosis can also impair oxygen transfer to the fetus via utero-placental vasoconstriction [16]. These changes are usually well-tolerated in healthy parturients with normal pregnancies.
Maternal transcutaneous PO2 as low as 44 mmHg has been observed during contractions [17]. Epidural analgesia reverses the adverse ventilatory effects of pain [18] and results in an increase in oxygen tension in both mother and fetus [19], which may be beneficial, especially when additional conditions contributing to fetal or maternal hypoxemia are also present.

**Neurohumoral effects** — Neurohumoral responses to stress and pain may adversely affect placental perfusion and fetal oxygenation. Studies in sheep demonstrated that pain increased circulating catecholamines and significantly decreased blood flow to the uterus [20]. In pregnant primates, stress and pain were shown to lower fetal oxygenation, cause fetal acidosis, and slow fetal heart rate. These changes may be of clinical concern when other conditions contributing to fetal hypoxemia are also present.

Removal of the stressful stimulus or sedation with pentobarbital or nitrous oxide reversed these changes [21]. The adverse effect of elevated circulating levels of epinephrine induced by maternal agitation and anxiety on fetal heart rate has also been documented in humans [22]. Epidural analgesia results in decreased concentrations of circulating maternal epinephrine, probably by reducing maternal pain and anxiety [23]. Epidural analgesia also results in a reduction of plasma beta-endorphin and cortisol levels [24].

**Psychological effects** — In addition to untoward physiological effects, unrelieved pain may also be a factor that contributes to the development of postpartum psychological trauma. Women who experience unrelieved pain during childbirth may be more likely to develop postpartum depression [25]. In a study of 1288 women following vaginal or cesarean delivery, the severity of acute postpartum pain, rather than the mode of delivery, correlated with the incidence of postpartum depression [26]. A more severe form of postpartum psychological trauma is posttraumatic stress disorder (PTSD). The prevalence of PTSD after childbirth has been reported to range from 1.7 to 6.9 percent [27]. A larger percentage of postpartum women develop some posttraumatic stress symptoms, but not the full-blown disorder. Although the etiology of PTSD is complex and multifactorial, unrelieved pain during childbirth has been identified as a risk factor for its development [28]. The profoundly harmful effects of postpartum PTSD on new mothers should not be underestimated [29].

**ANALGESIA FOR THE FIRST STAGE OF LABOR** — Pharmacologic approaches to manage childbirth pain can be broadly classified as either systemic or locoregional. Systemic administration includes the intravenous, intramuscular, and inhalation routes. Regional techniques (neuraxial) consist of epidurals, spinals and combined spinal-epidurals, and are the most popular modalities for analgesia for childbirth. Neuraxial techniques are widely acknowledged to be the only consistently effective means of relieving the pain of labor and delivery. Local injection may also be administered to achieve paracervical or pudendal nerve block. (See "Pudendal and paracervical block".)

**Systemic analgesics** — Systemic analgesics are useful for patients who prefer less invasive techniques, or in whom regional techniques are contraindicated, or are not an option due to lack of availability of skilled providers. The most popular systemic agents are opioids (eg, morphine, fentanyl, meperidine) or mixed opioid agonists-antagonists (eg, nalbuphine, butorphanol). Opioids exert their effects in the maternal brain, although a portion of the dose also crosses the placenta and affects the fetus. This is manifested in
utero by decreased fetal heart rate variability and in the neonate by respiratory depression [30,31].

Although systemic analgesics provide an alternative to regional analgesia, they are not as effective and produce respiratory depression. In laboring women, systemic opioids such as meperidine produce relief by inducing somnolence rather than by producing analgesia per se [32]. In a study of morphine and meperidine, repeated intravenous administration resulted in increasing sedation scores in parturients with little change in pain scores [33].

A list of systemic analgesics used in labor and delivery is provided in the table (table 2).

A systematic review of randomized trials of parenteral opioids for labor pain relief noted considerable heterogeneity among studies and many limitations to data interpretation (eg, low power, methodology issues) [34]. The major findings were:

- Satisfaction with pain relief provided by opioids during labor was low and only slightly better than placebo (29 versus 17 percent, p = 0.04). There was no evidence that any opioid was significantly more effective than meperidine, which is widely available and inexpensive. However, side effect profiles differed.

- Epidural analgesia provided better pain relief than parenteral opioids. However, opioids were associated with a shorter duration of labor and less oxytocin augmentation. Although opioids were also associated with fewer instrumental deliveries compared to epidural analgesia, only two trials evaluated this outcome. Furthermore, higher concentrations of local anesthetics, relative to current mixtures, were utilized in these trials.

- Nausea, vomiting, and sedation were common maternal side effects. Respiratory depression was the major neonatal concern; further investigation is required regarding possible long-term effects [35].

High doses of opioids are usually needed to obtain good pain relief; however, at these dosages maternal aspiration and maternal and neonatal respiratory depression are significant concerns. Parenteral opioids decrease fetal heart rate variability; therefore, consideration of alternative analgesic methods is useful when the fetus is at high risk for or demonstrates a nonreassuring fetal heart rate [5].

**Classic opioid analgesics** — The most commonly prescribed systemic opioid for labor pain relief worldwide is meperidine, a synthetic opioid [34]. However, its use has fallen into disfavor in the United States and there is a movement to replace meperidine with more efficacious and less toxic opioid analgesics because of its potential side effects (eg, serotonergic crisis, seizures and normeperidine toxicity) and multiple drug interactions (eg, MAO inhibitors). Morphine is a less popular choice, but is occasionally used to provide labor analgesia. However, the lack of efficacy of these medications and their associated maternal and neonatal side effects have resulted in decreased usage in many labor units where superior means of analgesia, such as regional techniques, are available [33,36].

Meperidine reaches a maximal concentration in the fetus between two and three hours after maternal dosing. As a result, classic teaching became that the neonate should be delivered within one hour or greater than four hours after a meperidine dose. Timing of delivery, however, is difficult to predict with precision. In addition, the metabolite normeperidine has
pharmacologic activity and a prolonged half-life in the neonate (2.5 days) [37], thus it may affect neonatal behavior [38] and difficulty with breastfeeding regardless of the timing of maternal administration [39].

**Newer opioid analgesics** — Fentanyl, a synthetic opioid, and its congeners (eg, sufentanil, alfentanil, and remifentanil) have also been used to provide labor pain relief. These drugs have a short duration of action, so they are best administered using the intravenous, rather than the intramuscular route. Of these agents, only fentanyl and remifentanil are suited for systemic labor analgesia [40].

Theoretically, the opioid best suited for providing labor analgesia using a systemic approach is a drug such as remifentanil, which is metabolized by nonspecific plasma and tissue esterases. Remifentanil rapidly transfers across the placenta, but is metabolized rapidly in the fetus and thus should not produce neonatal depression [41]. Its rapid onset of action, within one minute following intravenous injection, is another advantage for the parturient. For these reasons, remifentanil is gaining popularity for providing analgesia for childbirth in parturients in whom regional analgesia is either contraindicated or not desired [40,42-44], but further studies are needed to refine the methodology for its safe administration [45].

**Opioids with mixed agonist-antagonist properties** — Mixed opioid agonist-antagonists (eg, nalbuphine, butorphanol, pentazocine, and buprenorphine) for pain relief have the advantage of a dose ceiling effect with regard to respiratory depression. Butorphanol, for example, at doses greater than 10 mg intensifies analgesia without producing greater respiratory depression. These agents are associated with opioid side effects in the mother and fetus; psychotomimetic effects are particularly disconcerting.

**Patient controlled analgesia (PCA)** — Although the efficacy of intravenous PCA does not match that of regional analgesia, PCA is an appropriate choice for the parturient in whom neuraxial analgesia is contraindicated, or if the woman refuses neuraxial instrumentation.

PCA provides rapid onset of analgesia, fine control of pain relative to side effects, and psychological independence for the patient. Fentanyl is a familiar opioid and a popular choice, with a typical regimen being a 50 to 100 mcg loading dose and a patient-controlled dose of 20 to 60 mcg every 5 to 10 minutes. Remifentanil, due to its rapid onset and rapid metabolism, is increasingly being used to provide labor analgesia.

Various intravenous PCA regimens for remifentanil have been reported to provide analgesia during labor, with basal infusions ranging from 0 to 0.05 mcg/kg/min, bolus doses of 25 to 50 mcg, and lockout times of one to five minutes [40]. Although some data indicate that remifentanil is generally well-tolerated [46], it is prudent to monitor the parturient and her neonate for hypoxemia when intravenous PCA remifentanil is used since the drug is a potent respiratory depressant that may produce sedation and hypoxemia [47,48]. A practical problem of using remifentanil is that very brief lockout intervals (one to five minutes) are required, a shorter interval than is permitted by some standard PCA pumps. If any intravenous opioid is administered, maternal respiration must be continually monitored, because these agents are potent respiratory depressants.

**Nonopioid agents** — The most commonly used non-opioid agents are promethazine, a phenothiazine, and hydroxyzine, an antihistamine. These drugs are often administered in combination with an opioid to potentiate analgesia and decrease side effects, such as
nausea and vomiting.

Barbiturates such as **pentobarbital** and **secobarbital** are hypnotics and anxiolytics, not analgesics. They may be administered orally and are sometimes prescribed by obstetricians to enable a patient to sleep through early labor.

**Scopolamine** is a muscarinic anticholinergic drug that induces a dissociative state. Scopolamine was used in combination with an opioid for "twilight sleep", a technique popularized at the beginning of the 20th century, but it causes delirium and extreme agitation, sedation, and amnesia, and is rarely used for labor analgesia today.

**Ketamine** is a phencyclidine derivative that produces a dissociative state and analgesia. It is a potent amnestic, and has a rapid onset of action (less than one minute after intravenous administration). Ketamine tends to preserve airway reflexes, but also increases airway secretions, which may lead to laryngospasm. Its propensity to produce psychotomimetic effects may be prevented with coadministration of benzodiazepines. Ketamine will induce general anesthesia at doses of 1 mg/kg, but lower doses may be used to provide analgesia for vaginal delivery or minor operative procedures, such as manual uterine exploration. Doses above 1 mg/kg may cause uterine hypertonicity and decrease uteroplacental perfusion.

Benzodiazepines (eg, **midazolam** and **diazepam**) are anxiolytics that may be used for sedation during vaginal delivery. Midazolam is preferred because it is nonirritating to veins, and has a short duration of action. Similar to ketamine, benzodiazepines are potent amnestics that may impair the mother's memory of the birth if administered during labor. In addition, airway reflexes are obtunded, which is a risk factor for aspiration, especially since parturients in labor typically have increased gastric contents and delayed gastric emptying. Ketamine and benzodiazepines undergo placental passage and may result in neonatal depression.

**Nitrous oxide** — Nitrous oxide inhalation analgesia (blended of 50% nitric oxide and 50% oxygen gas) for labor pain is used in Great Britain, Scandinavia, Australia, Canada, and other countries, although it is rarely used in the United States [49]. The parturient self-administers the anesthetic gas, as needed, using a hand-held face mask. The safety of this technique is that the parturient will be unable to hold the mask if she becomes too drowsy, and thus will cease to inhale the anesthetic. Furthermore, it can be used at any stage of labor as it takes effect within 50 seconds and is eliminated quickly via the lungs so it does not accumulate in the mother or fetus/neonate or cause newborn depression. A disadvantage is that efficient scavenging is difficult with self-administered inhalation agents, resulting in environmental pollution.

A systematic review on nitrous oxide for relief of labor pain concluded that it was inexpensive, easy to administer, and safe for both mother and fetus/neonate [50]. The analgesic effect was better than that produced by opioids, but less than with epidural analgesia.

**Local injection techniques** — The pain of the first and second stages of labor may be ameliorated by injection of anesthetics locally. The obstetrical provider usually performs these injections. (See "Pudendal and paracervical block".)

**Neuraxial analgesia** — Neuraxial techniques provide unparalleled pain relief for labor and
delivery. In the United States, spinals and epidurals are used by more than 70 percent of women who give birth in hospitals with greater than 1500 deliveries per year [51]. Medical indications for neuraxial analgesia include anticipated difficulty with intubation, history of malignant hyperthermia, some cardiovascular and respiratory disorders, and prevention of autonomic hyperreflexia in women with a high spinal cord lesion [5]. Neuraxial anesthesia is preferred for women with preeclampsia [5].

Absolute contraindications to neuraxial analgesia include patient refusal, uncorrected coagulopathy (due to risk of spinal/epidural hematoma), infection of the lower back (due to risk of seeding of the neuraxis with bacteria), uncorrected hypovolemia (due to risk of profound hypotension from sympathetic block), and increased intracranial pressure (due to risk of herniation of the cerebral contents through the foramen magnum if dural puncture were to occur).

**Epidural techniques** — Local anesthetics, such as 0.03 to 0.125 percent bupivacaine or 0.075 to 0.2 percent ropivacaine, administered via the epidural route using continuous infusion pumps, provide safe and effective labor analgesia. The higher concentrations (eg, 0.125 percent bupivacaine or 0.2 percent ropivacaine) may be used alone, but for lower concentrations of local anesthetics to be effective (eg, as part of an "ultra-low dose" technique), they must be combined with other analgesics, most commonly neuraxial opioids. Neuraxial opioids alone, whether delivered by the intrathecal or epidural route, also provide excellent analgesia for the early first stage of labor. However, opioids alone do not reliably block the somatic pain component of late first stage (transition) or second stage of labor. A popular approach is to administer a combination of local anesthetic and opioid by continuous epidural infusion throughout labor. Most anesthesiologists use relatively lipid soluble synthetic opioids (eg, fentanyl or sufentanil) to reduce the high incidence of side effects seen with epidural morphine. Typical formulations for continuous epidural analgesia are bupivacaine 0.04 to 0.125 percent or ropivacaine 0.1 to 0.2 percent combined with fentanyl 0.5 to 3 mcg/mL or sufentanil 0.25 to 1 mcg/mL.

Some practitioners add epinephrine to the mix. Epinephrine enhances analgesia by activating neuraxial alpha-2 receptors, thus permitting a reduction in the concentration of local anesthetic administered. This reduction offsets an undesirable effect of epinephrine, namely its tendency to intensify local anesthetic-induced motor block. A benefit of adding epinephrine is that it may help to identify an unintentional intravascular injection, increasing maternal heart rate through its beta-1 agonist effects. Some practitioners use a small volume of concentrated local anesthetic containing epinephrine as a test dose after inserting the epidural catheter (eg, 3 mL lidocaine 1.5 percent with 1:200,000 epinephrine) to rule out intravascular or intrathecal placement. Others forego the test dose because "ultra-low dose" analgesic formulations are unlikely to result in toxicity, even if accidentally injected intravascularly or intrathecally. Also, administration of a relatively high concentration of local anesthetic in the test dose is likely to produce unwanted motor block, and unintended intravascular injection of the epinephrine component may decrease placental blood flow due to alpha adrenergic mediated uterine arterial constriction [52].

Moreover, wide fluctuations in maternal heart rate that occur during labor may mask epinephrine-induced increases in heart rate. Use of a baseline-to-peak increase greater than 10 beats/minute has been shown to eliminate this problem [53]. (See "Adverse effects of neuraxial analgesia and anesthesia for obstetrics".) Infusion pumps are commonly used
to facilitate continuous epidural drug administration. A typical regimen includes a loading dose of 10 to 20 mL, followed by an hourly infusion of 5 to 10 mL. If patient-controlled epidural analgesia (PCEA) is also used, patients may then self-administer doses at set intervals (eg, 3 to 10 mL every 10 to 30 minutes).

Breakthrough pain that occurs during continuous epidural infusion may be managed by administering a bolus dose of the infusate, and perhaps by increasing the basal rate of the infusion and/or by administration of a more concentrated dose of anesthetic as a "rescue dose," such as 3 to 6 mL of 0.25 percent bupivacaine every 15 minutes as needed until the parturient is comfortable. Ropivacaine 0.2 percent may be used instead of bupivacaine in this situation, but concentrated doses of lidocaine (eg, 1.5 to 2 percent) are best avoided, as they tend to cause a more intense motor block than do bupivacaine or ropivacaine.

With epidural techniques, "ultra-low dose" concentrations of local anesthetics may not be adequate to relieve the intense pain of the second stage of labor, as local anesthetic requirements increase as labor progresses [54]. For parturients who have epidural analgesia initiated late in labor (ie, during the late first stage ["transition"] or during the second stage), a higher concentration anesthetic (eg, 3 to 6 mL 0.25 percent bupivacaine) should be added to the initial 10 to 20 mL loading dose of "ultra-low dose" local anesthetic. Additional 3 to 6 mL doses of 0.25 percent bupivacaine may be administered as needed if pain persists after 15 minutes.

**Spinal techniques** — Spinal or combined spinal-epidural (CSE) techniques may also be used to relieve labor pain. Intrathecal analgesia with opioid alone (eg, 5 to 10 mcg sufentanil or 10 to 20 mcg fentanyl) during very early labor permits ambulation because spinal opioids have no effect on muscle strength. The intrathecal approach is also useful for the painful contractions of late first stage ("transition") because onset of analgesia is faster than with the epidural approach. Analgesia for the relatively severe pain of transition may be more reliably achieved by combining a small dose of local anesthetic (eg, 2 to 2.5 mg isobaric bupivacaine with an opioid, eg, 5 to 10 mcg sufentanil or 10 to 20 mcg fentanyl).

Compared to epidural techniques, spinal techniques have a more rapid onset: the patient is typically comfortable within five minutes. However, the pain relief is relatively short-lived, approximately 90 minutes. This is because catheters for administering additional doses of analgesics are usually not inserted into the intrathecal space. Therefore, if delivery is not imminent, a CSE technique is preferred.

The advantage of the CSE technique is that the epidural catheter may be activated if delivery has not occurred before the intrathecal dose wears off, if the spinal medication does not produce adequate analgesia, or if an instrumental or operative delivery is required. Most practitioners start the epidural infusion immediately following the CSE because it has been demonstrated that this approach produces longer analgesia compared to starting the infusion at the time of patient request [55]. On the other hand, compared to low-dose epidural techniques, spinal administration of opioids is associated with a greater incidence of fetal bradycardia and pruritus [56]. The fetal bradycardia is associated with uterine hypertonus, and is postulated to be due to a transient catecholamine imbalance. This imbalance involves an acute decrease in epinephrine levels with loss of epinephrine's tocolytic effect, and a relative increase in the uterotonic effect of norepinephrine. Catecholamine imbalance is not as likely to occur with epidural analgesia, which has a slower onset of action than spinal analgesia [57].
Spinal administration of local anesthetics may also induce maternal hypotension due to sympathectomy, but lower doses of local anesthetics should reduce this likelihood. However, maternal hypotension may also occur after administration of intrathecal opioids alone, presumably due to rapid onset of pain relief, and an acute decrease in circulating catecholamine levels, as intrathecal opioid administration (with the exception of meperidine) does not produce a sympathectomy per se [58]. (See "Adverse effects of neuraxial analgesia and anesthesia for obstetrics").

ANALGESIA/ANESTHESIA FOR THE SECOND STAGE OF LABOR

Continuation of epidural infusion — If a continuous epidural technique or patient controlled epidural analgesia (PCEA) is used for the first stage of labor, the volume of infusate is often sufficient to produce the sacral analgesia needed for the second stage. Ideally, the parturient maintains motor strength and senses pressure during the second stage, and the epidural infusion is continued to provide analgesia through delivery. However, if motor block is too intense and if a pressure sensation is not appreciated, the infusion may need to be stopped temporarily or decreased and the motor block allowed to dissipate. If this is done, the parturient should be encouraged to begin pushing as the effect wanes, but before the pain returns.

Some obstetricians prefer to discontinue epidural analgesia late in labor in the hope of decreasing the likelihood of instrumental delivery. A systematic review of this subject found insufficient evidence to support this practice, but did show that discontinuing epidural analgesia increases the rate of inadequate pain relief in the second stage of labor [59]. (See "Adverse effects of neuraxial analgesia and anesthesia for obstetrics", section on 'Potential benefits of delayed pushing'.)

Initiation of analgesia — There are situations in which neuraxial analgesia is not initiated until the second stage of labor. The parturient may not have desired neuraxial block earlier in labor or the fetal heart rate tracing or position may necessitate an instrumental delivery (eg, forceps or vacuum). Initiation of epidural analgesia is possible at this juncture, but the prolonged latency may make this choice less desirable than a spinal technique. Contraindications are the same as those listed above (see 'Neuraxial analgesia' above).

If an epidural is used, ultra-low concentrations of local anesthetics will likely be insufficient to relieve the intense pain of the second stage. We empirically add 3 mL 0.25 percent bupivacaine to the standard high volume (20 mL) low-concentration formulation of bupivacaine/sufentanil/epinephrine administered; additional 3 mL doses are given if pain persists after 15 minutes. Another reasonable option for providing second stage analgesia is to perform a spinal or CSE using a local anesthetic-opioid combination (eg, 2 mg isobaric bupivacaine and 5 mcg sufentanil given intrathecally). This has a rapid onset: the patient is typically comfortable within five minutes.

Pudendal nerve block — Bilateral pudendal nerve blocks are useful for alleviating pain arising from vaginal and perineal distention during the second stage of labor. They may be used as a supplement for epidural analgesia if the sacral nerves are not sufficiently anesthetized. Pudendal nerve blocks may also be performed to provide analgesia for low forceps, but they are inadequate for mid-forceps delivery. (See "Pudendal and paracervical block".)
Anesthesia for urgent situations — Obstetric complications occurring during the second stage of labor (eg, shoulder dystocia or entrapment of the fetal head with breech presentations) may require urgent anesthetic intervention. If a working epidural or spinal is not in place, it may be necessary to induce general anesthesia. A rapid sequence induction is indicated due to the "full stomach" status of parturients. The trachea is quickly intubated with a cuffed endotracheal tube to protect the lungs from aspiration of gastric contents. (See "Anesthesia for cesarean delivery").

Induction of general anesthesia and inhalation of a high concentration of volatile anesthetic will produce rapid uterine relaxation, facilitating delivery of an entrapped fetal head. However, if the parturient has a functioning regional anesthetic, intravenous administration of a low dose of the smooth muscle relaxant nitroglycerin (eg, 50 mcg) may be used to produce uterine relaxation [60] and facilitate delivery without exposing the parturient to the risks of induction of general anesthesia. Hypotension resulting from the nitroglycerin may be treated with small doses of ephedrine or phenylephrine. Intravenous nitroglycerin is also indicated for other situations in which uterine relaxation is desirable without the need for general anesthesia, such as retained placenta or uterine inversion.

SUMMARY AND RECOMMENDATIONS

- There are a variety of pharmacological options to manage the pain of parturition. Opioids administered systemically act primarily by inducing somnolence, rather than by producing analgesia per se. Moreover, placental transfer of opioids to the fetus may produce neonatal respiratory depression. If systemic opioids are used, they are optimally delivered with an intravenous patient-controlled analgesia (PCA) regimen. Systemic opioids may be the only option in settings with limited resources, or if regional analgesia (epidural and/or spinal) is contraindicated.

- Regional analgesic techniques, epidurals, spinals, and combined spinal-epidurals (CSE) are the most reliable means of relieving the pain of labor and delivery. By blocking the maternal stress response, epidural and spinal analgesia may reverse the untoward physiological consequences of labor pain. A distinct advantage of inserting an epidural catheter is that it may be used to administer anesthetics to provide pain relief for instrumental or cesarean delivery, if required. We recommend use of regional analgesia to manage the pain of labor and delivery for parturients desiring pharmacologic analgesia, in the absence of a contraindication. Furthermore, unless delivery is imminent, we recommend that an epidural catheter be inserted as a component of the regional technique.

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REFERENCES


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### Potential effects of severe labor pain

<table>
<thead>
<tr>
<th>Effect</th>
</tr>
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<tbody>
<tr>
<td>Increased oxygen consumption</td>
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<tr>
<td>Hyperventilation leading to hypocarbia and respiratory alkalosis</td>
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<tr>
<td>Gastric inhibition</td>
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<td>Increased gastric acidity</td>
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<tr>
<td>Lipolysis</td>
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<tr>
<td>Increased peripheral vascular resistance, cardiac output, blood pressure</td>
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<tr>
<td>Decreased placental perfusion</td>
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<tr>
<td>Incoordinate uterine activity</td>
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<tr>
<td>Postpartum psychological effects, such as posttraumatic stress disorder</td>
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</tbody>
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**Systemic analgesics used for labor and vaginal delivery**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
<th>Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meperidine</td>
<td>Opioid</td>
<td>25-50 mg IV</td>
<td>5 min IV</td>
<td>2-3 hr</td>
<td>Active metabolite is normeperidine a potent respiratory depressant; neonatal effect most likely if delivery occurs between 1 and 4 hr after administration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50-100 mg IM</td>
<td>40 min IM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>Opioid</td>
<td>2-5 mg IV</td>
<td>3-5 min IV</td>
<td>3-4 hr</td>
<td>Infrequent use during labor; greater respiratory depression in neonate than meperidine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5-10 mg IM</td>
<td>20-40 min IM</td>
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<td></td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Opioid</td>
<td>25-50 mcg IV</td>
<td>1-3 min IV</td>
<td>30-60 min IV</td>
<td>Short-acting, potent respiratory depressant; best used by PCA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100 mcg IM</td>
<td>7-10 min IM</td>
<td>1-2 hr IM</td>
<td></td>
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<tr>
<td>Nalbuphine</td>
<td>Mixed opioid agonist/antagonist</td>
<td>10-20 mg IV</td>
<td>2-3 min IV</td>
<td>3-6 hr</td>
<td>Agonist/antagonist; less nausea and vomiting than with meperidine; ceiling of respiratory depression</td>
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<tr>
<td></td>
<td></td>
<td>10-20 mg IM</td>
<td>10-15 min IM</td>
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<tr>
<td>Butorphanol</td>
<td>Mixed opioid agonist/antagonist</td>
<td>1-2 mg IV or IM</td>
<td>5-10 min IV</td>
<td>3-4 hr</td>
<td>Agonist/antagonist; maternal sedation similar to meperidine + phenothiazine; ceiling of respiratory depression; dysphoria</td>
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<td></td>
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<td>10-15 min IM</td>
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<tr>
<td>Pentazocine (Talwin)</td>
<td>Mixed opioid agonist/antagonist</td>
<td>20-40 mg IV/IM</td>
<td>2-3 min IV</td>
<td>2-3 hr</td>
<td>Agonist/antagonist; ceiling of respiratory depression; dysphoria</td>
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<td></td>
<td></td>
<td>5-20 min IM</td>
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<tr>
<td>Promethazine (Phenergan)</td>
<td>Phenothiazine</td>
<td>25-75 mg IV/IM</td>
<td>10-20 min</td>
<td>3-4 hr</td>
<td>Commonly used with opioids to mitigate nausea &amp; vomiting; may produce hypotension</td>
</tr>
<tr>
<td>Hydroxyzine (Vistaril)</td>
<td>Antihistamine</td>
<td>25-50 mg IM</td>
<td>30 min</td>
<td>4 hr</td>
<td>Commonly used with opioids to mitigate nausea &amp;</td>
</tr>
<tr>
<td>Drug</td>
<td>Class</td>
<td>Dose/Route</td>
<td>Onset</td>
<td>Duration</td>
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<tr>
<td>Pentobarbital (Nembutal)</td>
<td>Barbiturate</td>
<td>100-200 mg PO/IM</td>
<td>30-60 min</td>
<td>3-6 hr</td>
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<tr>
<td>Vomiting; not used IV (painful on injection)</td>
<td>Hypnotic; used only in early or prodromal labor</td>
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<tr>
<td>Secobarbital (Seconal)</td>
<td>Barbiturate</td>
<td>100 mg PO</td>
<td>30-60 min</td>
<td>3-6 hr</td>
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<tr>
<td>Vomiting; not used IV (painful on injection)</td>
<td>Hypnotic; used only in early or prodromal labor</td>
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<tr>
<td>Ketamine (Ketalar®)</td>
<td>Phencyclidine derivative</td>
<td>10-20 mg IV</td>
<td>&lt;1 min</td>
<td>5 min</td>
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<tr>
<td>IV dose should not exceed 1 mg/kg per 30 min; psychiatric effects may be prevented with concomitant benzodiazepine; sedation for vaginal delivery; potent amnestic and analgesic</td>
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<tr>
<td>Midazolam (Versed)</td>
<td>Benzodiazepine</td>
<td>1-5 mg IV</td>
<td>3-5 min</td>
<td>1-2 hr</td>
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<tr>
<td>Sedation and anxiolysis for vaginal delivery; non-irritating when given IV; potent amnestic; rapid onset/offset; used for eclamptic seizures</td>
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<tr>
<td>Diazepam (Valium)</td>
<td>Benzodiazepine</td>
<td>2-5 mg IV</td>
<td>5 min</td>
<td>1-2 hr IV</td>
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<tr>
<td>10 mg IM</td>
<td>3-4 hr IM</td>
<td>Sedation and anxiolysis for vaginal delivery; potent amnestic; rapid onset/offset; prolonged half-life; used for eclamptic seizures</td>
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</tbody>
</table>