CLINICAL THERAPEUTICS

Epidural Analgesia for Labor and Delivery

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This Journal *feature begins with a case vignette that includes a therapeutic recommendation. A discussion of the clinical problem and the mechanism of benefit of this form of therapy follows. Major clinical studies, the clinical use of this therapy, and potential adverse effects are reviewed. Relevant formal guidelines, if they exist, are presented. The article ends with the author's clinical recommendations.*

A 30-year-old nulliparous woman at 39 weeks' gestation is undergoing induction of labor because of premature rupture of membranes. She is currently receiving an oxytocin infusion, and her cervical dilatation is 1 cm. Her obstetrician has ordered intermittent intravenous administration of fentanyl for pain relief, but she feels nauseated, has been unable to rest, and describes her pain as 9 on a scale of 10. The patient strongly prefers a vaginal delivery to cesarean delivery and is concerned that epidural analgesia may alter the progress of labor. The anesthesiologist is consulted to discuss the use of epidural analgesia during labor and delivery.

THE CLINICAL PROBLEM

For most women labor causes severe pain, similar in degree to that caused by complex regional pain syndromes or the amputation of a finger.[1] The American College of Obstetricians and Gynecologists and the American Society of Anesthesiologists (ASA) state, "There is no other circumstance where it is considered acceptable for an individual to experience untreated severe pain, amenable to safe intervention, while under a physician's care. In the absence of a medical contraindication, maternal request is a sufficient medical indication for pain relief during labor."[2]

Although severe pain is not life-threatening in healthy parturient women, it can have neuropsychological consequences. Postnatal depression may be more common when analgesia is not used,[3] and pain during labor has been correlated with the development of post-traumatic stress disorder.[4] In addition, one study suggested that the impairment of cognitive function in the postpartum period can be mitigated by the use of any form of intrapartum analgesia.[5] Men are also affected by severe labor pain. A survey of first-time fathers showed that the men whose partners received an epidural felt three times as helpful and involved during labor and delivery and had less anxiety and stress, as compared with men whose partners did not receive an epidural.[6]

PATHOPHYSIOLOGY AND THE EFFECT OF THERAPY

The pain of labor, caused by uterine contractions and cervical dilatation, is transmitted through visceral afferent (sympathetic) nerves entering the spinal cord from T10 through L1 (Fig. 1). Later in labor, perineal stretching transmits painful stimuli through the pudendal nerve and sacral nerves S2 through S4. The maternal stress response can lead to increased release of corticotropin, cortisol, norepinephrine, β-endorphins, and epinephrine. Epinephrine can have relaxant effects on the uterus that may prolong labor. Studies in healthy pregnant ewes showed that psychological stress or pain increased maternal plasma levels of norepinephrine by 25%

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and decreased uterine blood flow by 50%.[7] Catecholamine release is also accompanied by increased maternal cardiac output, systemic vascular resistance, and oxygen consumption. For women with preexisting cardiac or respiratory compromise, such increases may be difficult to sustain.

Epidural analgesia for labor and delivery involves the injection of a local anesthetic agent (e.g., lidocaine or bupivacaine) and an opioid analgesic agent (e.g., morphine or fentanyl) into the lumbar epidural space (Fig. 2).[8] The injected agent gradually diffuses across the dura into the subarachnoid space, where it acts primarily on the spinal nerve roots and to a lesser degree on the spinal cord and paravertebral nerves. In spinal analgesia, which is often combined with epidural analgesia, the analgesic agent is injected directly into the subarachnoid space, resulting in a more rapid onset of effect.[8]

Successful epidural analgesia produces a segmental sympathetic and sensory nerve block and a decrease in endogenous catecholamines with the onset of pain relief.[9] Hypotension or normalization of blood pressure to prelabor levels may occur with vasodilatation, which may result from sympathetic nerve blockade and a decrease in circulating catecholamines. However, if blood pressure is maintained, the reduction in vascular resistance results in a statistically significant improvement in uteroplacental blood flow in both healthy patients[10] and those with severe preeclampsia.[11] The degree of the motor-neuron effect depends on the concentration of local anesthetic. However, neuraxial local anesthetics in clinically relevant doses affect only skeletal muscle, not smooth muscle; these agents do not decrease the amplitude or frequency of contractions in the myometrium.[12]

Figure 1 (facing page). Sources of Pain during Labor and Maternal Physiological Responses.

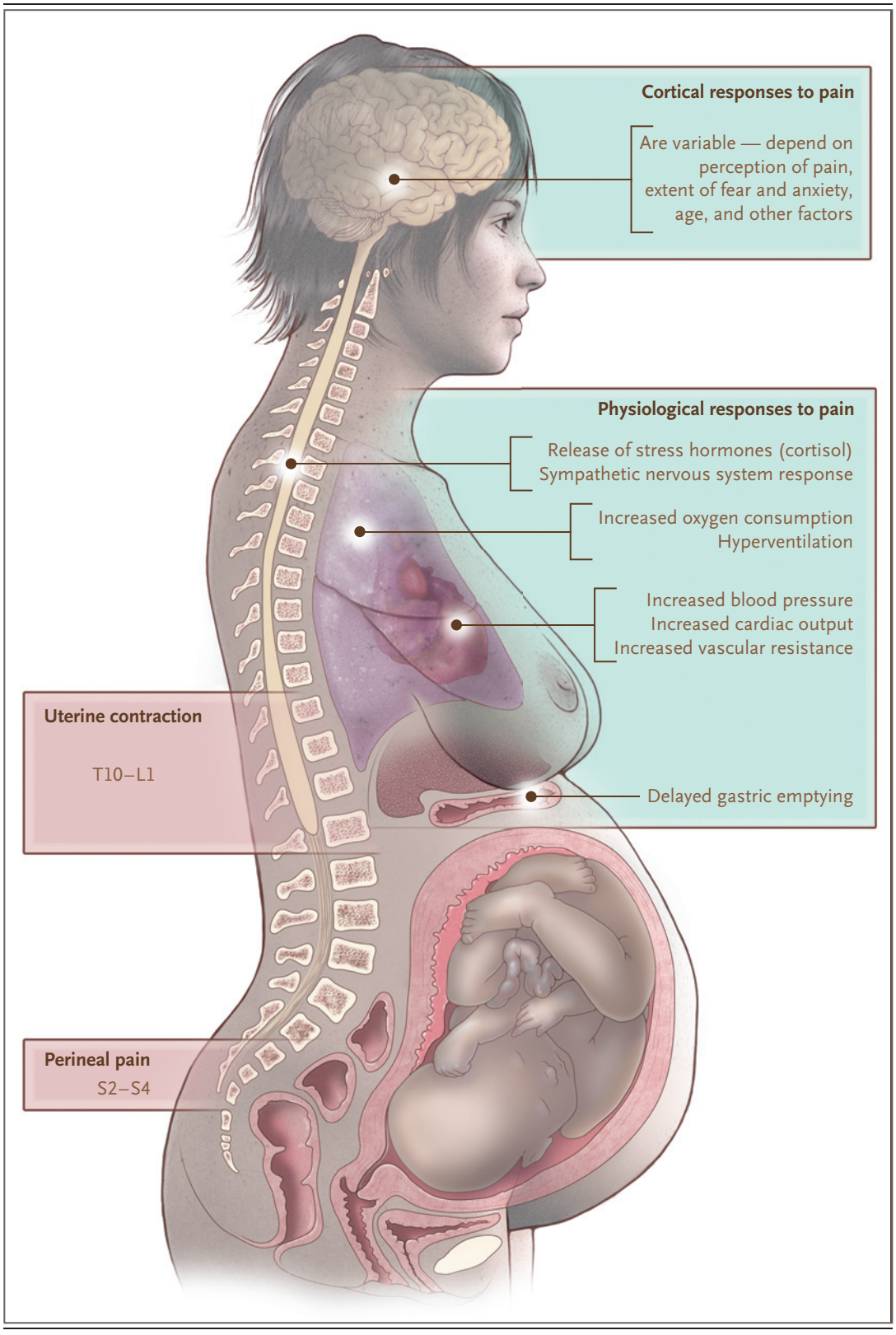
The pain of labor, caused by uterine contractions and cervical dilatation, is transmitted through visceral afferent (sympathetic) nerves entering the spinal cord from T10 through L1. Later in labor, perineal stretching transmits painful stimuli through the pudendal nerve and sacral nerves S2 through S4. Cortical responses to pain and anxiety during labor are complex and may be influenced by the mother's expectations for her childbirth experience, her preparation (through education), the presence of emotional support, her age, and other factors. The perception of pain is increased by fear and anxiety. Coping behaviors may include verbalization and the need to move into various positions. She may be motivated to have a certain type of birthing experience, and these opinions will influence her judgment about pain management and other choices during labor and delivery. Maternal physiological responses to labor pain may influence maternal and fetal well-being and the progress of labor. Hyperventilation may induce hypocarbia. An increased metabolic rate increases oxygen consumption. Increases in cardiac output and vascular resistance may increase maternal blood pressure. Pain, stress, and anxiety cause release of stress hormones such as cortisol and β-endorphins. The sympathetic nervous system response to pain results in a marked increase in circulating catecholamines, such as norepinephrine and epinephrine, that can adversely affect uterine activity and uteroplacental blood flow. Effective analgesia attenuates or eliminates these responses.

CLINICAL EVIDENCE

Randomized, controlled trials of the effects of analgesia administered during labor are difficult to conduct. It is problematic to randomly assign women to a placebo (no pain relief) and would be considered unethical in most circumstances, if epidural analgesia was available and there was no opportunity for crossover. Most trials have compared the use of epidural analgesia with that of systemic narcotics such as intravenously administered fentanyl or meperidine that is controlled by the patient. Blinding is difficult, and rates of crossover from opioids to neuraxial analgesia are high.[13]

In one large trial, 992 nulliparous women were randomly assigned to either epidural analgesia or continuous midwifery support (supplemented by intramuscular administration of meperidine, nitrous oxide inhalation, or nonpharmacologic methods of pain relief).[14] When pain was rated on a scale of 0 to 100, with 100 being the worst pain imaginable, the median scores before the study interventions were 80 in the group assigned to midwifery support and 85 in the group assigned to epidural analgesia. With the administration of epidural analgesia, the median score was reduced to 27, as compared with 75 during the provision of midwifery support ($P<0.001$).

In another study, a meta-analysis involving 2703 nulliparous women enrolled in five trials conducted at a single institution,[15] the participants had been randomly assigned to either epidural analgesia or intravenous administration of meperidine. On the basis of a visual-analogue pain



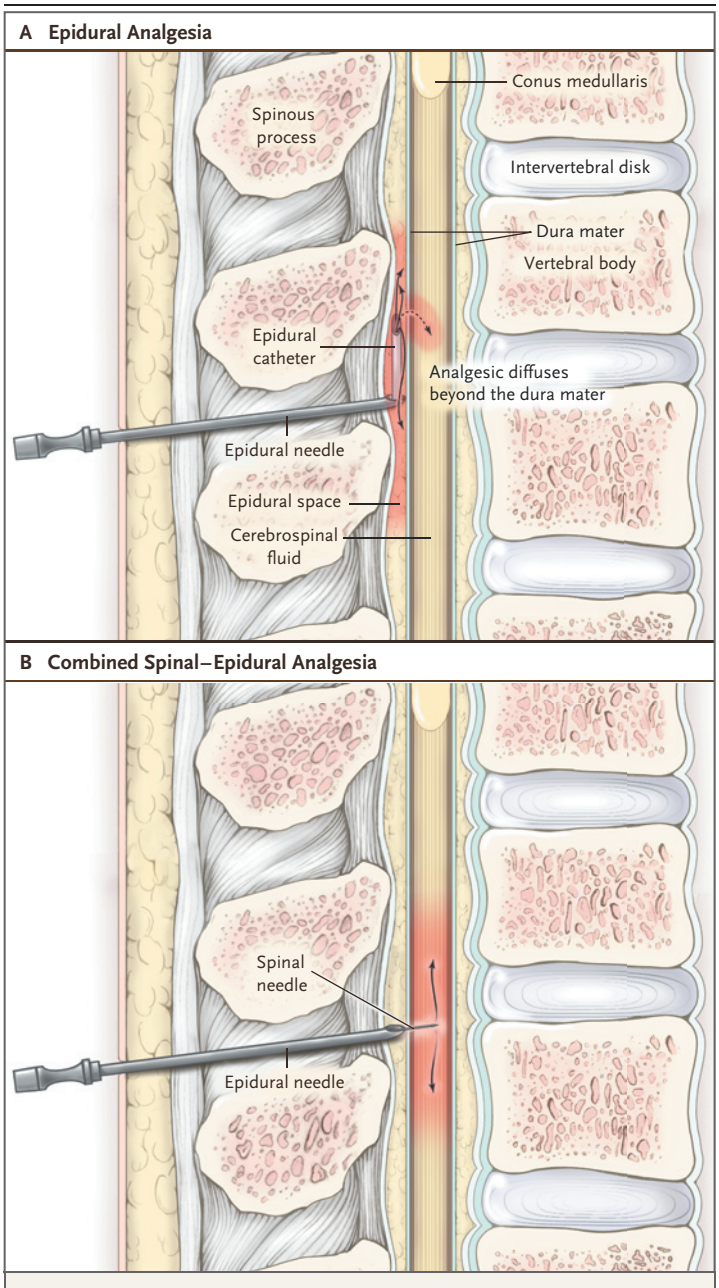


Figure 2. Epidural Analgesia versus Combined Spinal–Epidural Analgesia.
In the initiation of epidural analgesia for labor and delivery (Panel A), a local anesthetic agent and an opioid analgesic agent are injected into the lumbar epidural space, where they gradually diffuse across the dura into the subarachnoid space, acting on spinal nerve roots, the spinal cord, and paravertebral nerves. A small catheter is then passed through the epidural needle to provide continuous access to the epidural space for maintenance of analgesia throughout labor and delivery. In combined spinal–epidural analgesia (Panel B), an alternative method of initiating analgesia during labor, a small-gauge, "pencil-point" spinal needle is passed through the epidural needle into the cerebrospinal fluid, and a small dose of opioid, with or without local anesthetic, is injected. After injection, the spinal needle is withdrawn and an epidural catheter is inserted into the epidural space for maintenance of analgesia.

scale ranging from 0 to 10 (with 10 representing the worst pain), both the epidural and meperidine groups had a mean preanalgesia score of 9. The mean score fell to 2 in the epidural group and 4 in the meperidine group ($P<0.001$) during the first stage of labor and rose to 3 and 5, respectively ($P<0.001$), during the second stage of labor. On the first postpartum day, 95% of women in the epidural group reported their satisfaction with pain relief during delivery as excellent or good, as compared with 69% of women in the meperidine group ($P<0.001$).

CLINICAL USE

Pain management is an essential part of good obstetrical care, although not all women request analgesia during labor and delivery. The obstetrical provider should discuss the options with the patient, but the decision should be based on the patient's preference. Many effective options are available for the management of pain during labor, including systemic opioids and alternative nonpharmacologic options, such as sterile water injections,[16] acupuncture,[17] assistance from a doula (a person with training in labor support),[18] and water therapy in showers or whirlpool baths.[19] These techniques are often used by women early in labor, even if epidural analgesia is requested at a later time.

When a woman requests epidural analgesia for labor, she should have a preprocedural evaluation by the anesthesiologist, who will also obtain informed consent. Contraindications for neuraxial (spinal or epidural) techniques are clinically significant coagulopathy (including ongoing thromboprophylaxis with low-molecular-weight or unfractionated heparins),[20] uncorrected maternal hypovolemia, infection at the needle-puncture site, increased intracranial pressure that could lead to herniation if dural puncture occurred, and inadequate training or experience on the part of those providing the anesthesia.

At the time of placement of the nerve block, emergency equipment must be immediately available to treat serious untoward reactions. These can include hypotension, respiratory compromise, and in rare cases, seizures and cardiac arrest. Precautions taken to prevent infection include removal of jewelry, careful hand washing, use of a fresh face mask, and disinfection of the patient's back with 2% chlorhexidine in alcohol.[21]

The epidural space is located with the use of

the "loss of resistance" technique.[22] A lumbar vertebral space is chosen below the L1 vertebra, where the spinal cord ends in most adults. The meeting point of lines drawn from each iliac crest serves to locate the L4 spinous process. An epidural needle attached to a syringe of air or saline is advanced slowly through spinal ligaments as pressure is applied to the syringe plunger. Resistance to plunger pressure is lost on entry into the epidural space (Fig. 2). If placement is difficult (e.g., because the patient is obese), ultrasound guidance can be used to identify the midline and other anatomical landmarks, the depth of the epidural space, and the intervertebral space.[23]

Once the epidural space has been entered, an epidural catheter is threaded through the needle and into the space. The epidural needle is then withdrawn, leaving the catheter in place. Incremental boluses of the selected analgesic agent are administered through the epidural catheter. A local anesthetic is typically combined with an opioid for this purpose. The quality of the analgesia is improved with the combined use of a local anesthetic and an opioid as compared with the use of either agent alone. This approach also reduces the dose of each agent needed (limiting toxicity), prolongs the analgesic effect, reduces motor block, and improves patient satisfaction, as compared with the use of local anesthetic alone. Examples of combinations that provide excellent sensory block with relatively little motor block include 0.125% bupivacaine or 0.1% ropivacaine with 5 μg of fentanyl per milliliter or 1 μg of sufentanil per milliliter.

A second option for inducing analgesia is to pass a 25-to-27-gauge "pencil-point" spinal needle through the epidural needle (using it as an introducer), puncture the dura, and inject a small dose of opioid, with or without local anesthetic, into the spinal fluid. The spinal needle is then withdrawn, and the epidural catheter is placed through the epidural needle as described above. This approach is called combined spinal–epidural analgesia.

The choice of using an epidural bolus or a spinal dose (combined spinal–epidural) to initiate the block is based largely on the provider's preference. Spinal opioids provide excellent analgesia without motor block in early labor, which is useful for women who want to walk (sometimes referred to as the walking epidural) or to allow for labor in positions other than the supine position. In addition, the onset of spinal analgesia is more rapid than that of epidural analgesia, and spread to the sacral nerve roots is more reliable, making spinal analgesia useful in advanced, rapidly progressing labor. However, the overall outcomes and complications associated with the epidural technique and the combined spinal–epidural technique are similar.[24]

Maintenance of analgesia can be achieved by allowing continuous infusion of dilute local anesthetic and opioid agents through the epidural catheter or by giving the patient control of intermittent bolus administration. The benefits of the patient-controlled technique include greater patient satisfaction, fewer interventions by an anesthetist, reduced requirement for a local anesthetic, and reduced motor block.[25] Most regimens combine a basal infusion rate with patient-controlled boluses.[26] Effective infusion rates may vary, depending on individual variations in the response to pain, the stage of labor (early vs. advanced), and the patient's expectations for her childbirth experience. Rates may be increased in cases of inadequate pain control and decreased when there is excessive motor block.

Maternal blood pressure should be monitored intermittently, and fetal heart rate intermittently or continuously, throughout the course of anesthesia administration. During maternal positioning for placement of the epidural catheter, continuous fetal monitoring may not be possible without the use of a fetal scalp electrode.[27] The extent of dermatomal sensory loss and of motor block should be evaluated regularly after block initiation and while the infusion is being administered. Respiratory monitoring should be performed every hour.[28] If the patient wishes to get out of bed after epidural placement, her orthostatic vital signs and motor strength must be normal.

The epidural infusion is discontinued after delivery, and the catheter removed. There is no benefit in discontinuing the infusion during the second stage of labor, while the patient is pushing, although motor block should be minimized throughout labor by adjusting the infusion rate. If cesarean delivery is required, the epidural catheter can be used to provide anesthesia with a more concentrated local anesthetic.

When used for labor and delivery, epidural analgesia is estimated to be slightly more costly than intravenous analgesia. In one U.S. study published in 2002, the estimated cost of a vaginal delivery with the use of intravenous analgesia was $3,117;

with epidural analgesia, the estimated cost was $3,455.[29]

ADVERSE EFFECTS

There has been a good deal of concern, based on older observational studies, that women who have epidural analgesia during labor are more likely to require a cesarean delivery.[30] However, the preponderance of evidence now supports the conclusion that the use of epidural analgesia during labor does not have a significant effect on rates of cesarean delivery. A Cochrane review of 20 trials involving a total of 6534 women estimated that the relative risk of cesarean delivery with epidural analgesia as compared with other methods or with no analgesia was 1.07 (95% confidence interval, 0.93 to 1.23).[31] Epidural analgesia does increase the duration of the second stage of labor by 15 to 30 minutes and may increase the rate of instrument-assisted vaginal deliveries as well as that of oxytocin administration.[32,33] Clinicians and patients have also been concerned about whether the use of epidural analgesia in early labor increases the risk of cesarean delivery. Three randomized, controlled trials showed that early initiation of epidural analgesia (cervical dilatation, <4 cm) does not increase the rate of cesarean delivery among women with spontaneous or induced labor, as compared with early initiation of analgesia with parenteral opioids.[34-36]

Nonreassuring fetal heart tones during labor have been reported in 10 to 20% of patients after initiation of neuraxial analgesia, although adverse neonatal outcomes have not been reported.[37] Hypertonic uterine contractions may occur more often after the administration of spinal opioids than after an epidural and are probably the result of a rapid decrease in plasma levels of epinephrine (i.e., reduced β-agonist tocolytic activity) brought on by the very rapid onset of analgesia.[38] Uterine relaxation can be accomplished with the intravenous administration of 250 μg of terbutaline or 50 to 150 μg of nitroglycerin or with the administration of 400 μg of nitroglycerin as a sublingual spray. Urinary retention during epidural analgesia is common, but it can be minimized by avoiding dense motor and sensory blocks.[39] A systematic review of serious adverse events among 1.37 million women receiving epidural analgesia during labor showed that the risks of epidural hematoma and epidural abscess were 1 case per 168,000 women and 1 per 145,000, respectively; the risk of persistent neurologic injury was 1 case per 240,000 women, and the risk of transient neurologic injury was 1 per 6700.[40]

Hypotension affects up to 80% of parturient women, and there is no reliable way to prevent it, although uterine displacement, fluid administration, and treatment with pressors may mitigate the severity. Although usually self-limited, hypotension should be treated promptly to prevent decreases in uteroplacental perfusion; 50 to 100 μg of phenylephrine or 5 to 10 mg of ephedrine (the choice depending on maternal heart rate), administered with intermittent boluses, is recommended.

Unintentional intrathecal injection of large doses of local anesthetic can cause a high spinal block, leading to respiratory compromise, and unintentional intravenous injection can lead to high blood levels of local anesthetic, resulting in seizures and cardiac arrest. Emergency equipment must always be immediately available.[27] Intravenous lipid emulsion has emerged as an effective therapy for cardiotoxic effects of lipid-soluble local anesthetics such as bupivacaine or ropivacaine. Such therapy should be available whenever regional anesthesia is provided.[41,42]

Headache may occur after dural puncture, usually when the dura has been unintentionally punctured with the typical 17- or 18-gauge epidural needle, which is known as a wet tap. The incidence of wet tap is about 1%, with subsequent headache developing in about 70% of cases. Approximately half these cases of headache require an epidural blood patch, in which sterile injection is used to introduce 15 to 25 ml of the patient's blood into the epidural space; treatment is successful in 65 to 90% of cases.[43] Although patients are often concerned about back pain after epidural analgesia, the incidence of long-term back pain is not increased after the administration of epidural anesthesia as compared with the use of parenteral opioids or of no analgesia during labor.[44]

AREAS OF UNCERTAINTY

Two areas of uncertainty related to epidural analgesia are its associations with maternal fever and reduced success in breast-feeding. Epidural-associated fever has been reported in randomized, controlled trials, but the mechanism is unknown.[45] Maternal fever may cause neonatologists to perform evaluation for sepsis in the newborn, although the incidence of sepsis in infants does not

differ according to whether epidural analgesia was used during labor.[46] Fetal hyperthermia at term is associated with an increased risk of neonatal encephalopathy and cerebral palsy, so the goal is to prevent fetal exposure to intrauterine hyperthermia from any cause.[47] There is no evidence that epidural analgesia is associated with cerebral palsy.

The association of epidural analgesia with reduced breast-feeding success is difficult to study because of the myriad medical and social variables that affect a woman's decision to initiate or continue breast-feeding her infant. Although retrospective studies conflict in their conclusions,[48,49] large doses of epidural fentanyl (>150 μg) given during the course of labor may interfere with early breast-feeding success; consequently, boluses and high infusion concentrations of fentanyl should be avoided.[50]

GUIDELINES

The Practice Guidelines for Obstetric Anesthesia from the ASA state, "The choice of analgesic technique depends on the medical status of the patient, progress of labor, and resources at the facility. When sufficient resources (e.g., anesthesia and nursing staff) are available, neuraxial catheter techniques should be one of the analgesic options offered."[27] The ASA has also published guidelines for the prevention, diagnosis, and management of infectious complications associated with neuraxial techniques.[51] These guidelines complement those from the American Society of Regional Anesthesia.[21] Measures that can be taken to reduce the incidence and severity of neuraxial, opioid-related respiratory depression are the subject of another ASA practice guideline.[28] The American College of Obstetricians and Gynecologists has issued an educational bulletin on obstetrical anesthesia and analgesia,[52] as well as a committee opinion refuting the association of epidural analgesia with increased cesarean-delivery rates.[53]

RECOMMENDATIONS

The woman described in the vignette is a good candidate for epidural analgesia. She should be advised that according to the best available evidence, epidural analgesia does not increase the risk of cesarean delivery. She should also be told that she is likely to have less nausea with epidural analgesia than with fentanyl. She may prefer use of a patient-controlled epidural pump during the maintenance phase of analgesia because this will allow her to optimize her pain relief. Minimizing motor and sensory block during her infusion may allow her to sit in a chair, stand at the bedside, or assume other positions in labor if desired, and it may also reduce her need for urinary catheterization and instrument-assisted delivery. If the need for cesarean delivery arises, the epidural catheter can be used to provide anesthesia for her surgery and postoperative pain management.

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Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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