

MEDICAL PROGRESS

Regional Anesthesia and Analgesia for Labor and Delivery

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IN 1847, THE SCOTTISH OBSTETRICIAN JAMES SIMPSON ADMINISTERED ether to a woman during labor to treat the pain of childbirth. He was impressed with the degree of analgesia associated with the use of the drug. Nevertheless, he expressed concern about the possible adverse effects of anesthesia: "It will be necessary to ascertain anesthesia's precise effect, both upon the action of the uterus and on the assistant abdominal muscles; its influence, if any, upon the child; whether it has a tendency to hemorrhage or other complications."¹

One and a half centuries later, the maternal and fetal effects of analgesia during labor remain central to discussions among patients, anesthesiologists, and obstetrical caregivers. A number of randomized trials have sought to address the effects of different strategies for analgesia on maternal and fetal outcomes. Despite this effort, it has become increasingly clear that potentially unwanted effects of analgesia for women in labor and their children cannot be determined easily. Remaining controversies in obstetrical anesthesia include that over the effects of regional anesthesia on the progress and outcome of labor, as well as that over its effects on the neonate. In this article we will concentrate on advances in the administration of epidural, spinal, or combined spinal–epidural analgesia during labor. However, there are many other methods of pain management that may be chosen by women in labor, such as opioids,² hydrotherapy, hypnotherapy, the use of labor-support personnel (doulas), massage, movement and positioning, and sterile-water blocks, among others.³ These alternative methods can be used successfully either alone or in conjunction with epidural analgesia. In addition, successful relief of labor pain in itself is not necessarily associated with high levels of satisfaction on the part of parturient women.^{4,5} Factors such as the woman's involvement in decision making, social and cultural factors, the woman's relationship with her caregivers, and her expectations regarding labor may be equally, if not more, important.

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REGIONAL ANALGESIA FOR VAGINAL DELIVERY

TECHNIQUE OF REGIONAL ANALGESIA

Approximately 60 percent of women, or 2.4 million each year, choose epidural or combined spinal–epidural analgesia for pain relief during labor.⁶ Labor pain is transmitted through lower thoracic, lumbar, and sacral nerve roots (Fig. 1 and 2) that are amenable to epidural blockade. Epidural analgesia is achieved by placement of a catheter into the lumbar epidural space. Solutions of a local anesthetic, opioid, or both can then be administered as intermittent rapid doses or as a continuous infusion (Fig. 3). The alternative technique of combined spinal–epidural analgesia has recently gained in popularity. With this technique, a single bolus of an opioid, sometimes in combination with local anesthetic, is injected into the subarachnoid space, in addition to the placement of an epidural catheter (Fig. 3). The use of a subarachnoid bolus of opioids results in the rap-

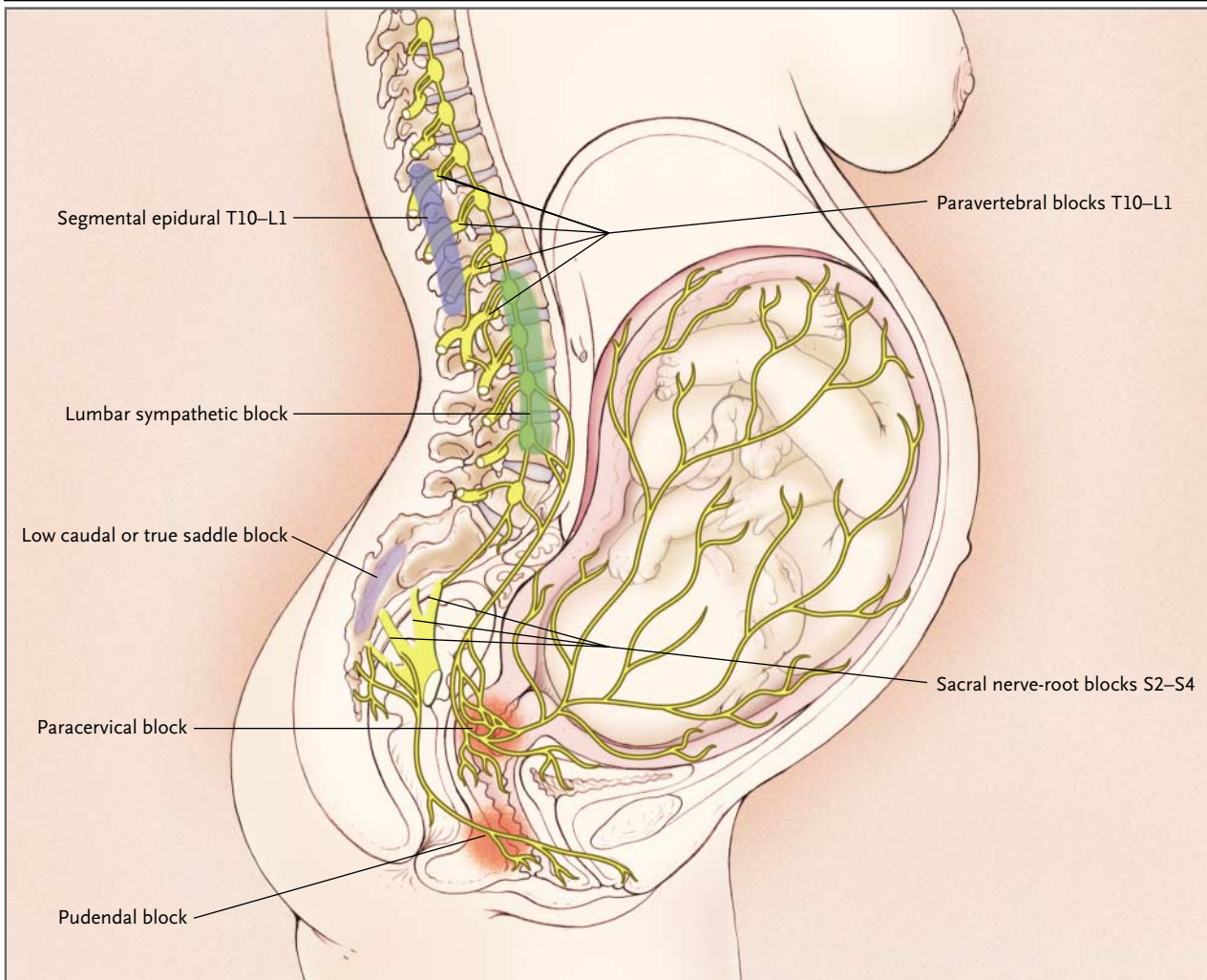


Figure 1. Pathways of Labor Pain.

Labor pain has a visceral component and a somatic component. Uterine contractions may result in myometrial ischemia, causing the release of potassium, bradykinin, histamine, and serotonin. In addition, stretching and distention of the lower segments of the uterus and the cervix stimulate mechanoreceptors. These noxious impulses follow sensory-nerve fibers that accompany sympathetic nerve endings, traveling through the paracervical region and the pelvic and hypogastric plexus to enter the lumbar sympathetic chain. Through the white rami communicantes of the T10, T11, T12, and L1 spinal nerves, they enter the dorsal horn of the spinal cord. These pathways could be mapped successfully by a demonstration that blockade at different levels along this path (sacral nerve-root blocks S2 through S4, pudendal block, paracervical block, low caudal or true saddle block, lumbar sympathetic block, segmental epidural blocks T10 through L1, and paravertebral blocks T10 through L1) can alleviate the visceral component of labor pain.

id onset of profound relief of pain with virtually no motor blockade. In contrast to epidural local anesthetics, spinal opioids do not cause impairment of balance, giving the parturient woman the option to continue ambulation.⁷ Combined spinal-epidural analgesia is associated with a higher degree of satisfaction among parturient women than is conventional epidural analgesia.⁸ However, some studies have suggested that there may be an increase in

the frequency of nonreassuring patterns in the fetal heart rate, particularly bradycardia, with combined spinal-epidural analgesia, and such patterns may necessitate emergency cesarean delivery.⁹⁻¹¹ Other studies show no difference in the fetal heart rate and no increase in the rate of cesarean deliveries necessitated by fetal bradycardia.^{12,13} Although there are insufficient data to establish whether there is a causal association, it is reassuring that no

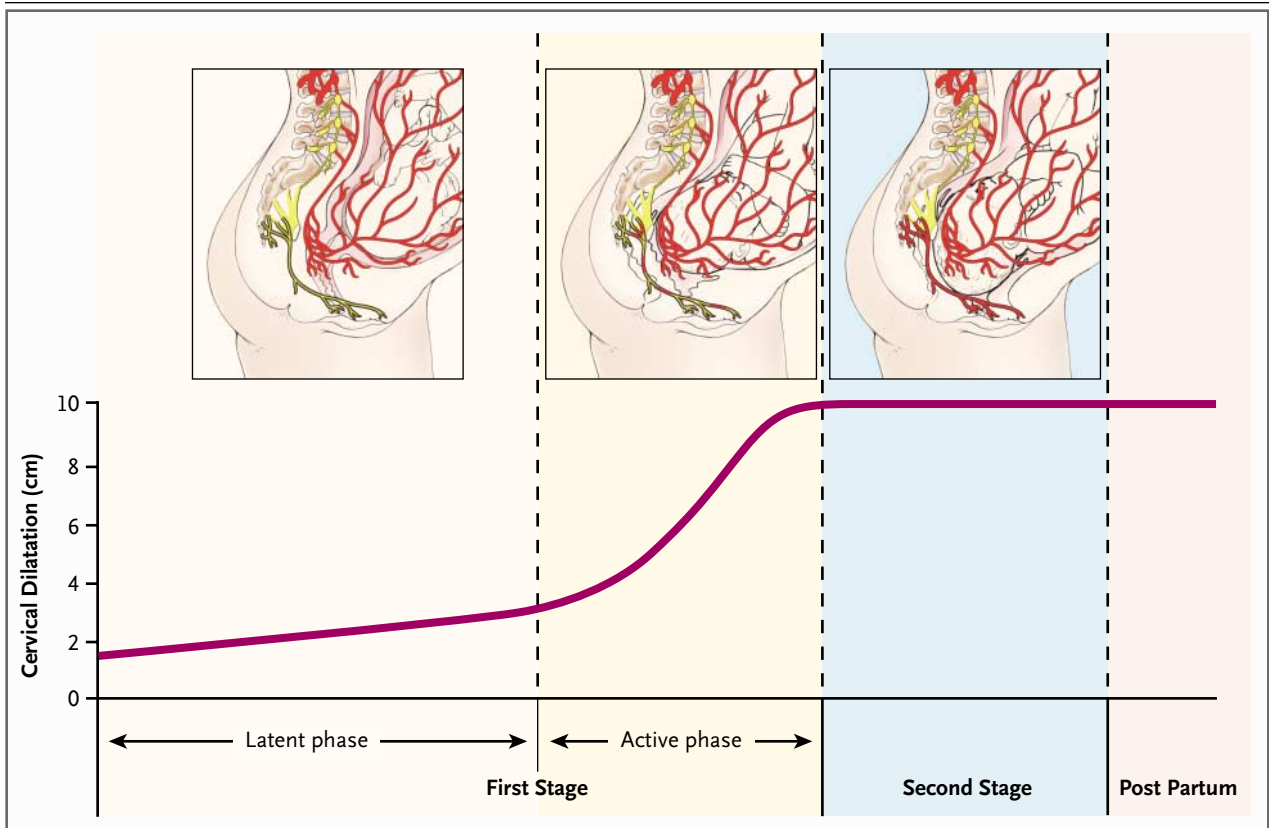


Figure 2. Labor Pain during Different Stages of Labor.

Traditionally, labor has been divided into three stages. The first stage is defined as that lasting from the start of regular uterine contractions until the completion of cervical dilatation. It is commonly subdivided into a latent and an active phase, the latter being characterized by a rapid acceleration of cervical dilatation. The second stage proceeds from the first stage until the delivery of the fetus is complete, and the third stage continues until the placenta and membranes have been expelled. Pain during the first stage of labor is visceral and is therefore mediated by the T10 through L1 segments of the spine, whereas during the later part of the first stage and throughout the second stage, an additional somatic component is present, mediated by the S1 through S4 segments of the spine. Active pain pathways are marked in red.

studies suggest that combined spinal–epidural analgesia is associated with an increase in adverse outcomes for the fetus.

EFFECT OF EPIDURAL ANALGESIA ON THE METHOD OF DELIVERY

The use of epidural analgesia is associated with better pain relief than are systemic opioids.¹⁴⁻¹⁷ However, a major concern is whether epidural analgesia may be responsible for an increased risk of cesarean delivery, vaginal delivery requiring the use of forceps or vacuum extraction, or prolongation of labor. Both cesarean deliveries and instrument-assisted vaginal deliveries may be associated with a greater risk of maternal complications than unassisted vaginal de-

livery. Although the appropriate rate of cesarean delivery remains a matter of debate¹⁸ (currently in the United States, the babies of 23 percent of pregnant women are delivered by cesarean section¹⁹), there is great interest in the effect of epidural analgesia on these rates. In addition, the rate of instrument-assisted vaginal delivery is of concern because it is consistently associated with a higher rate of serious perineal laceration,²⁰ which has been implicated as a risk factor for later fecal incontinence.²¹ Instrument-assisted vaginal deliveries have also been linked to higher rates of birth injuries.²²

OBSERVATIONAL STUDIES

Many studies compare women who selected epidural analgesia with those who did not. Most such

studies show an association between the use of epidural analgesia and a higher rate of cesarean delivery. However, women who select epidural analgesia are different from those who do not. They are more frequently nulliparous, come to the hospital earlier in the course of labor with the fetus having descended to a lesser degree (a higher fetal station), have slower cervical dilatation, deliver larger babies, and have smaller pelvic outlets.²³⁻²⁶ Observational studies that control for these factors continue to find differences in outcome between the women who receive epidural analgesia and those who do not.^{24,26} One observational study suggests that women with difficult labor may have more pain early in labor and require a more potent regimen for pain relief.²⁷

However, although the small subgroup of women with exceptionally painful labor may be more likely to choose epidural analgesia, this is clearly not the main factor contributing to the choice of a method of pain relief, since many women having a first baby decide before labor whether to receive epidural analgesia.²⁸ Overall, given the possibility of uncontrolled confounding, it is not possible to draw definitive conclusions from these observational studies.

RANDOMIZED TRIALS

Prospective, randomized trials studying the relation between the use of epidural analgesia and cesarean delivery have shown variable results. A recent meta-analysis represents the experience of nearly 2400 patients randomly assigned to receive either epidural analgesia or parenteral opioid analgesia.¹⁷ Epidural analgesia was associated with a prolongation of the first stage of labor by an average of 42 minutes and a prolongation of the second stage of labor by an average of 14 minutes. No significant difference between groups in the rate of cesarean delivery could

be demonstrated by intention-to-treat analysis (8.2 percent of women in the epidural group had cesarean deliveries, as compared with 5.6 percent in the parenteral-opioid group).

However, in most of the large studies, about 30 percent of women did not receive the treatment to which they were assigned. Many women assigned to the parenteral-opioid group actually received epidural analgesia, and many women assigned to receive epidural analgesia did not receive it. When such crossover occurs, the proportion of women who receive epidural analgesia in the two groups becomes much more similar, making it very difficult to interpret the data on an intention-to-treat basis. In many trials, a substantial proportion of women did not receive the assigned treatment because delivery occurred so rapidly that there was no time to administer any analgesia. In addition, women who agree to be randomly assigned to a certain form of pain relief during active labor may represent a subgroup of women with less difficult labors or other characteristics that render them unrepresentative of the general population. This high rate of non-compliance with the protocols limits our ability to interpret the data.²⁹

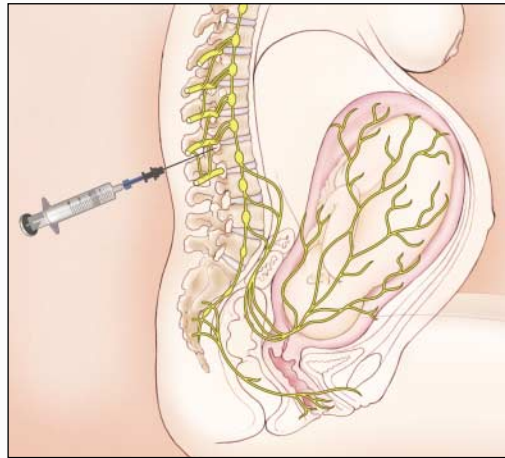
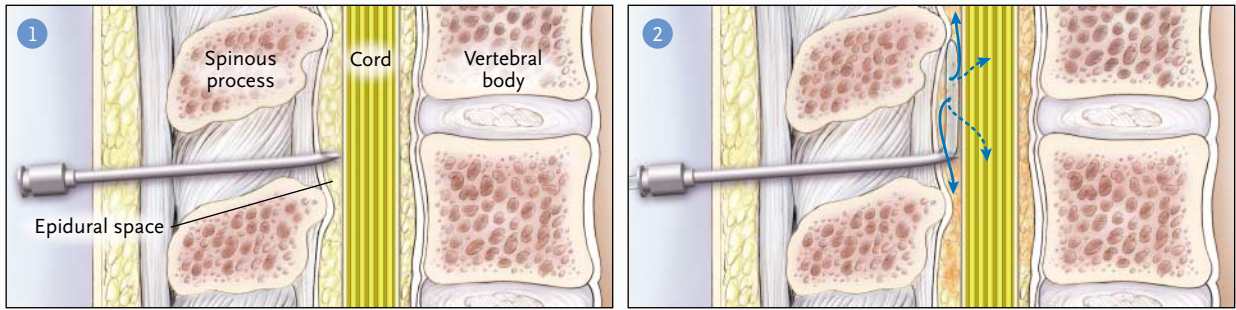
There have been two randomized trials with essentially no crossover. In the first trial, in which 93 nulliparous women in spontaneous labor at term were randomly assigned to epidural analgesia or parenteral meperidine, essentially all women received the assigned treatment. This study found a large effect of the use of epidural analgesia on the rate of cesarean deliveries performed because of dystocia (17 percent in the epidural group vs. 2 percent in the meperidine group).³⁰ In contrast, a more recent study,³¹ in which 459 nulliparous women in active labor were randomly assigned to either epi-

Figure 3 (facing page). Technique of Epidural Analgesia and Combined Spinal–Epidural Analgesia.

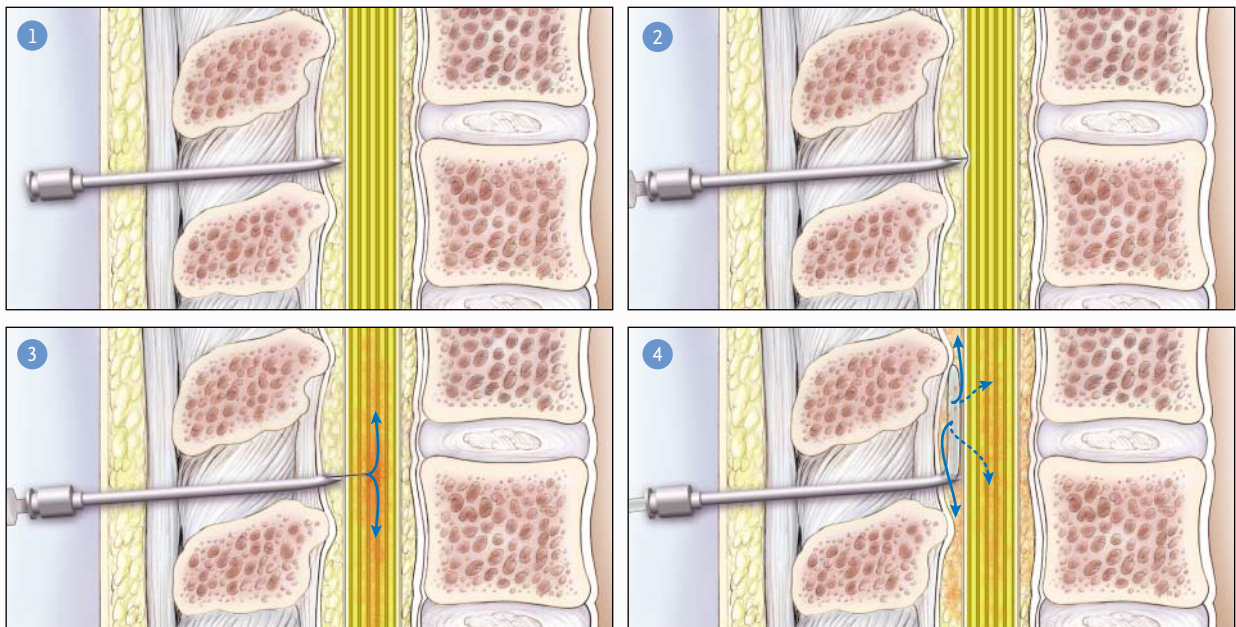
Epidural analgesia (Panel A) is achieved by placement of a catheter into the lumbar epidural space (1). After the desired intervertebral space (e.g., between L3 and L4) has been identified and infiltrated with local anesthetic, a hollow epidural needle is placed in the intervertebral ligaments. These ligaments are characterized by a high degree of resistance to penetration. A syringe connected to the epidural needle allows the anesthesiologist to confirm the resistance of these ligaments. In contrast, the epidural space has a low degree of resistance. When the anesthesiologist slowly advances the needle while feeling for resistance, he or she recognizes the epidural space by a sudden loss of resistance as the epidural needle enters the epidural space (2). Next, an epidural catheter is advanced into the space. Solutions of a local anesthetic, opioids, or a combination of the two can now be administered through the catheter.

For combined spinal–epidural analgesia (Panel B), the lumbar epidural space is also identified with an epidural needle (1). Next, a very thin spinal needle is introduced through the epidural needle into the subarachnoid space (2). Correct placement can be confirmed by free flow of cerebrospinal fluid. A single bolus of local anesthetic, opioid, or a combination of the two is injected through this needle into the subarachnoid space (3). Subsequently, the needle is removed, and a catheter is advanced into the epidural space through the epidural needle (4). When the single-shot spinal analgesic wears off, the epidural catheter can be used for the continuation of pain relief.

A Epidural Analgesia



B Combined Spinal–Epidural Analgesia



dural analgesia or intravenous meperidine and in which 8 percent of the subjects had protocol violations, found no significant difference in the rate of cesarean deliveries performed because of dystocia (6 percent in the epidural group vs. 7 percent in the meperidine group).

It is not clear why these two studies had such different results. It is important to note that the effect of epidural analgesia on the likelihood of cesarean delivery may vary according to obstetrical practice and the population studied and that such variations may be the reasons for the differences between the studies.^{32,33} Studies have clearly demonstrated great variations in physician-specific rates of cesarean delivery, suggesting that management practices may have an important role. For example, in a study of 1533 parturient women who were cared for by 11 obstetricians, the rate of cesarean delivery varied from 19 percent to 41 percent for different caregivers.³³ In addition, women enrolled in many of the randomized trials were much younger than the general population of women delivering babies in the United States.³⁴ Studies consistently demonstrate an increase in the rate of cesarean delivery associated with age,³⁵ and the effect of epidural analgesia may vary with age as well. Therefore, the question of whether the use of epidural analgesia for pain relief during labor increases the rate of cesarean deliveries performed because of a failure of labor to progress remains unanswered.

Findings with regard to an association between instrument-assisted vaginal delivery and epidural analgesia are clearer, with a consistent increase in the rates of deliveries involving forceps and vacuum extraction with epidural analgesia. The meta-analysis of randomized trials found a doubling of the rate of instrument-assisted vaginal deliveries.¹⁷ The most recent randomized trial found an increase in the rate of deliveries involving forceps from 3 percent in the opioid group to 12 percent in the epidural-analgesia group.³¹ However, the reason for this increase with epidural analgesia remains unclear. One hypothesis is that the motor blockade may prevent the mother from pushing and thereby necessitate the use of instruments. Epidural analgesia is also associated with a higher frequency of the occiput posterior position of the fetus at delivery, which, if causal, could represent a mechanism by which epidural analgesia contributes to the higher rate of instrument-assisted delivery.^{30,36,37} It is also possible that the presence of an epidural block may sometimes decrease the obstetrician's threshold for

performing instrument-assisted deliveries,¹⁷ as well as for allowing instrument-assisted delivery for the purposes of teaching residents.³⁷

STUDIES OF SENTINEL EVENTS

A different approach is taken to the question of epidural analgesia and cesarean delivery by studies comparing the rates of cesarean delivery before and after epidural analgesia was made available for a certain population of women. The assumption of such studies is that the population of women, the obstetrical management style, and other confounding variables change little over time. None of these studies have demonstrated an increase in the rate of cesarean delivery associated with the sudden availability of epidural analgesia.³⁸⁻⁴² A recent meta-analysis of these studies, which included more than 37,000 patients in a variety of different practice settings and time periods in several countries, showed that the establishment of a highly utilized epidural-analgesia service had no effect on the overall incidence of cesarean delivery or the rate of cesarean deliveries performed because of dystocia.⁴³

However, these studies have methodologic limitations. First, it is almost impossible to control for changes in practice style that may occur when an epidural-analgesia service is introduced; such changes may be made specifically because providers are aware of the potential association of epidural analgesia with an increased rate of cesarean deliveries. Second, there may be secular trends, such as overall changes in the rate of cesarean delivery between the two periods being studied. Finally, substantial changes may occur in the rate of cesarean delivery in subgroups of patients (e.g., nulliparous women in spontaneous labor) without causing a statistically detectable increase in the overall rate of cesarean delivery. It would be difficult with this type of study design to detect changes even in large subgroups of women. Therefore, these studies do not provide a conclusive answer to the question of the effects of epidural analgesia on outcomes of labor for individual women. However, they do show that the institution of an active anesthesia service providing epidural analgesia need not lead to an increase in the overall rate of cesarean delivery.

In summary, it appears that epidural analgesia may prolong labor by approximately one hour, on average. The effect on the rate of cesarean delivery is unclear and may vary with the practice-related choices of the provider.^{29,32,33} The literature does provide evidence of an increase in the rate of instrument-

assisted vaginal delivery and a decrease in the rate of spontaneous vaginal deliveries with epidural analgesia, although the reason for this association is not well understood, and the magnitude of the association may be influenced by the practice style of the obstetrician.

TIMING OF EPIDURAL ANALGESIA DURING LABOR

It has been suggested that the effect of epidural analgesia on labor and the method of delivery may be greater when such analgesia is administered before a certain degree of cervical dilatation or a certain fetal station has been reached. Most observational studies show higher rates of cesarean delivery with early administration of epidural analgesia.^{26,44,45} In contrast, the three randomized studies specifically comparing the initiation of epidural analgesia at different degrees of cervical dilatation in nulliparous women found no difference in the rate of cesarean delivery or instrument-assisted vaginal delivery between women in whom analgesia was initiated early and those in whom it was initiated late.⁴⁶⁻⁴⁸ However, the small degree of difference in cervical dilatation between the early and late groups (approximately 1 cm) is an important limitation of these trials. There is currently insufficient evidence to determine whether waiting until a certain degree of cervical dilatation or a certain fetal station is reached before instituting epidural analgesia will influence the rate of cesarean or instrument-assisted vaginal deliveries.

EFFECT OF COMBINED SPINAL-EPIDURAL ANALGESIA ON THE RATE OF CESAREAN DELIVERY

Since combined spinal-epidural analgesia is not associated with impaired equilibrium,⁷ ambulation during labor can be continued by up to 80 percent of parturient women.⁴⁹ It was therefore hypothesized that the use of combined spinal-epidural analgesia in association with continued ambulation might lead to a decrease in the rate of cesarean delivery. The results of major clinical trials did not support this hypothesis⁵⁰ or a positive effect of ambulation itself on the rate of cesarean delivery.⁵¹ However, a randomized trial did demonstrate that combined spinal-epidural analgesia is associated with more rapid cervical dilatation in nulliparous women than is conventional epidural analgesia, al-

though no difference in the rate of cesarean delivery was found.⁵²

EFFECT OF EPIDURAL ANALGESIA ON MATERNAL TEMPERATURE AND THE NEWBORN

Epidural anesthesia in nonobstetrical patients is generally associated with a decrease in body temperature. Epidural anesthesia causes vasodilatation in the anesthetized dermatomes, which leads to a redistribution of heat from the core to the periphery, resulting in a net decrease in body temperature.⁵³ In contrast, observational and randomized studies demonstrate that epidural analgesia during labor is often associated with an increase in maternal body temperature to over 100.4°F (38.0°C).⁵⁴⁻⁵⁶ For example, in a randomized trial in which fever was reported, an additional 11 percent of women receiving epidural analgesia became febrile during labor (15 percent, vs. 4 percent of women who received no epidural analgesia), and the proportion of the population affected was even greater among nulliparous women (24 percent vs. 5 percent).⁵⁵ An association between the use of epidural analgesia and maternal fever raises some important questions: Does epidural analgesia cause maternal or neonatal infections? Do children of mothers who receive epidural analgesia more frequently require evaluation for sepsis and treatment with antibiotics?

The association between the use of epidural analgesia and maternal fever is complex. Some authors assert that the increase in the frequency of fever is the result of placental infection, as assessed by neutrophilic infiltration of the placenta, possibly associated with the longer duration of labor among women who receive epidural analgesia.⁵⁷ This explanation seems unlikely to be correct, however, since women with long labors but no epidural analgesia do not tend to have such high rates of fever.⁵⁴ In addition, if infection were the cause, the incidence of neonatal sepsis would be expected to be higher among the infants of women who receive epidural analgesia. In fact, the rate of sepsis among term infants is equally low whether or not the mother receives epidural analgesia.

Many investigators believe the association of epidural analgesia with fever is probably attributable to noninfectious causes, such as an alteration in the production and dissipation of heat resulting from epidural analgesia.⁵⁶ Both randomized and observational studies have demonstrated that infants of

women who receive epidural analgesia are more likely to be evaluated and treated with antibiotics because of concern about infection.^{54,55} The higher rates of evaluation for sepsis are expected, since fever in labor raises concern about infection that may be passed to the neonate, and it is not currently possible to distinguish between fever from infectious causes and fever from noninfectious causes during labor.⁵⁴ The rates of evaluation for sepsis among infants of afebrile women depend on the criteria by which pediatricians determine which infants to evaluate.^{55,58} Observational studies have also noted an association between intrapartum maternal fever and other adverse neonatal outcomes, even when the infant does not have an infection.^{59,60}

A more complete understanding of the causes and physiological correlates of fever related to epidural analgesia and the development of markers to distinguish infectious from noninfectious causes of fever may provide a means of safely decreasing the number of evaluations for sepsis that are needed. It seems highly unlikely that such increases in temperature have an infectious cause, and neonates born to mothers who receive epidural analgesia do not have an increased risk of sepsis. Further study is needed to determine the best criteria for performing workups for sepsis in infants of low-risk women who deliver infants at term. Additional studies, particularly randomized trials, are also needed to examine further the reported adverse effects on the neonate of epidural-related fever in the mother during labor.

OTHER REPORTED COMPLICATIONS OF REGIONAL ANALGESIA

Many parturient women are concerned that epidural analgesia may lead to back pain. A recent randomized trial studied 385 nulliparous parturient women for 12 months after delivery.⁶¹ No difference in the incidence of backache could be demonstrated be-

tween women who were randomly assigned to receive epidural analgesia and those who were not. The results of several nonrandomized trials are consistent with these findings.^{62,63} Therefore, current data do not support a relation between a new onset of back pain and the use of epidural analgesia during labor.

Inadvertent puncture of the subarachnoid space during the placement of an epidural catheter occurs in about 3 percent of parturient women, and a severe headache occurs in up to 70 percent of women with such a puncture.⁶⁴ Postdural puncture headache can be treated with an epidural blood patch, which is effective in relieving headache in more than 75 percent of women.⁶⁵ If the headache does not have the pathognomonic postural characteristics or persists despite treatment with an epidural blood patch, other diagnoses should be considered and appropriate testing performed.⁶⁶

There are a number of other complications that have been reported in connection with epidural analgesia, including effects on the neonate, for which the available data are inadequate to allow definitive conclusions to be drawn. In addition, we do not know whether the use of epidural analgesia influences fetal position at delivery. Although it has been demonstrated that women who receive epidural analgesia are more likely to have a fetus in the occiput posterior position at delivery,^{30,36,37} it is not clear whether the use of epidural analgesia contributes to the persistence of this position or whether women with a fetus in this position have more painful labors and are therefore more likely to request epidural analgesia.

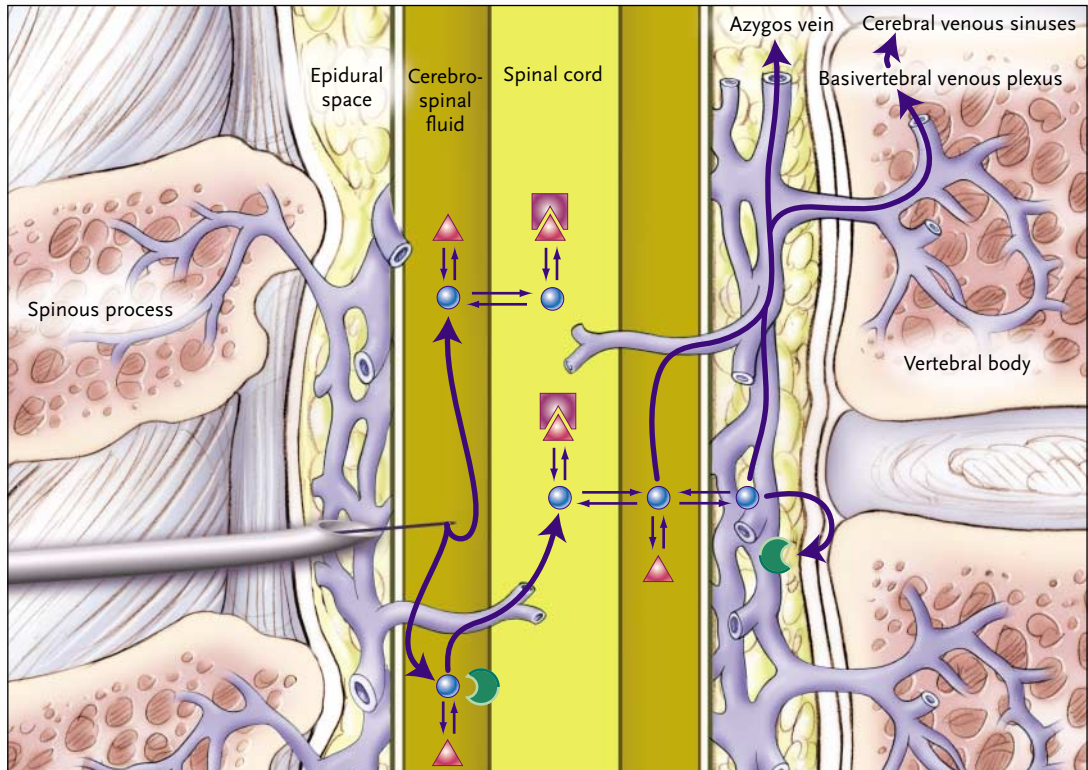
FASTING DURING LABOR AND DELIVERY

Historically, a dreaded complication of obstetrical anesthesia has been the so-called Mendelson's syndrome, the aspiration into the lungs of acid stom-

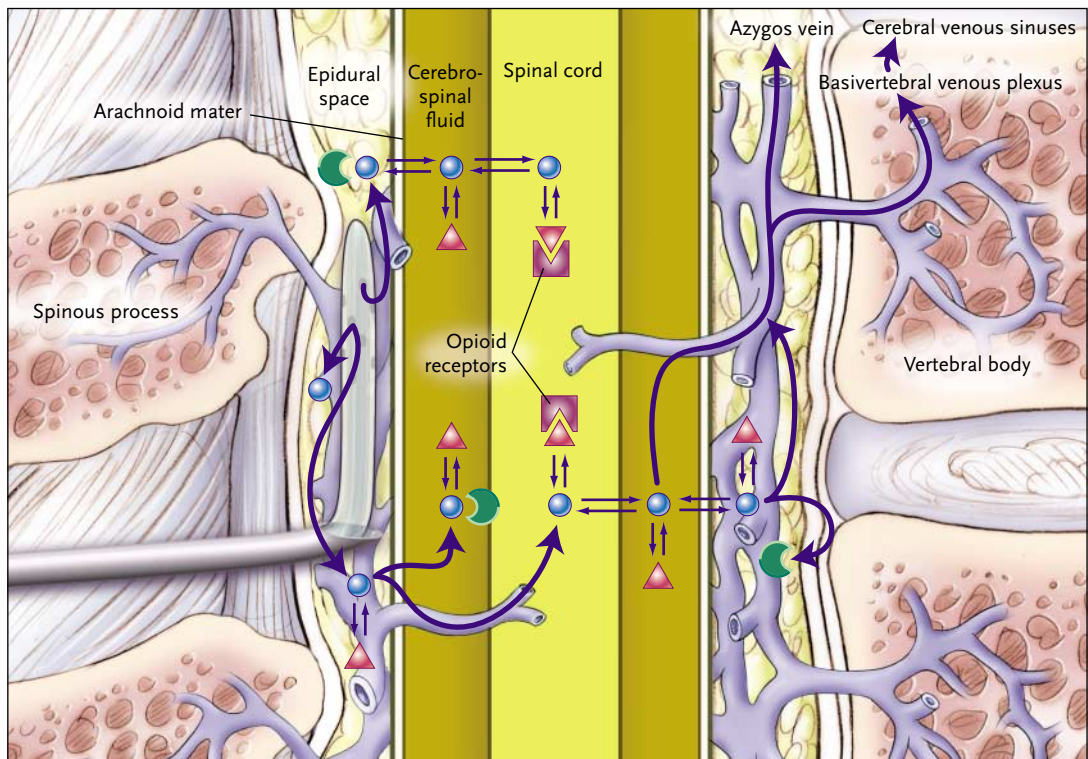
Figure 4 (facing page). Pharmacokinetics of Spinal and Epidural Opioids.

Panel A shows subarachnoid injection and Panel B epidural injection of a hydrophilic opioid such as morphine. A needle is shown delivering opioid directly into the cerebrospinal fluid (Panel A) or into the epidural space (Panel B). When a drug is administered epidurally, it can reach the spinal cord by diffusion through the meninges. The most important barrier to meningeal permeability is the arachnoid mater; meningeal permeability is determined primarily by the drug's lipid solubility. In the spinal cord, equilibrium of the nonionized hydrophilic drug (blue circles) and the ionized hydrophilic drug (red triangles) at the site of the spinal opioid receptor (purple receptors) is shown, as well as nonspecific lipid-binding sites (green receptors). Diffusion into the epidural space and into epidural veins is the major route of clearance, as illustrated in the left portion of the image.

A Spinal Opioids



B Epidural Opioids



ach contents.⁶⁷ To increase the safety of pain relief during labor and delivery, strict fasting policies have been instituted. However, with improvements in anesthetic and obstetrical management, the rate of death from aspiration has declined; the most recent data from the United States indicate that for every 10 million births, seven women die from aspiration.⁶⁸

Advances in analgesia permit the liberalization of requirements for fasting during labor. The practice guidelines of the American Society of Anesthesiologists recommend limited amounts of clear fluid during labor⁶⁹; this recommendation is supported by a recent study demonstrating that the use of isotonic sport drinks during labor has the potential to decrease the risk of maternal ketosis associated with starving without increasing gastric volume or the risk of nausea and vomiting.⁷⁰

PAIN RELIEF DURING AND AFTER CESAREAN DELIVERY

Uses of analgesia for cesarean delivery include the management of pain during surgery and the treatment of pain during the postoperative period. During the past decade, there has been a decrease in the use of general anesthesia and an increase in the use of regional techniques for the treatment of postoperative pain; neuraxially administered opioids for such pain have also been introduced.

GENERAL ANESTHESIA

General anesthesia is associated with a higher risk of airway problems among women undergoing cesarean delivery than among nonobstetrical patients. The incidence of failed tracheal intubation is estimated as 1 in 200 to 1 in 300 cases^{71,72} — almost 10 times as high as that among nonobstetrical patients.⁷³ Maternal death due to anesthesia is the sixth leading cause of pregnancy-related death in the United States.⁷⁴ Most anesthesia-related deaths occur during general anesthesia for cesarean delivery. The risk of maternal death from complications of general anesthesia is 17 times as high as that associated with regional anesthesia.⁶⁸ Recognition of the risks to the mother associated with general anesthesia has led to an increased use of spinal and epidural anesthesia for both elective and emergency cesarean deliveries.⁷⁵ This shift may be the most important reason for a decrease in anesthesia-associated maternal mortality from 4.3 to 1.7 per 1 million live births in the United States.⁶⁸ Even in cases in which the status of the fetus is not reassuring, a

technique of regional anesthesia may be preferable to general anesthesia. The obstetrical care team should be alert to important risk factors that place the parturient woman at a substantially increased risk for complications of the emergency use of general anesthesia, such as signs predicting a difficult intubation.⁷⁶ If such risk factors are present, a management plan should be developed jointly by obstetricians and anesthesiologists, and placement of an epidural or spinal catheter early in the course of labor should be considered. This approach is recommended by the Committee on Obstetric Practice of the American College of Obstetricians and Gynecologists.⁷⁶

POSTCESAREAN ANALGESIA

In 1976, data from experiments in rats revealed a direct spinal action of opioids,⁷⁷ and the first clinical use in 1979⁷⁸ was soon followed by application in the obstetrical field.⁷⁹ With selective activation of spinal opioid receptors, the dose required to produce anesthesia is decreased by more than 95 percent as compared with systemic application, and the frequency of opioid-induced side effects that are mediated by brain-stem opioid receptors is decreased. Women undergoing cesarean delivery can receive intrathecal or epidural morphine, which produces a clinically relevant reduction in postoperative pain over a 24-hour period (Fig. 4).⁸⁰⁻⁸²

Despite the specific activation of spinal opioid receptors, an activation of brain-stem opioid receptors either through systemic absorption and redistribution to the brain or by circulation of cerebrospinal fluid accounts for possible side effects such as pruritus, nausea and vomiting, and respiratory depression (Fig. 5). A recent meta-analysis reports a 43 percent incidence of pruritus after the administration of 0.1 mg of intrathecal morphine.⁸³ The effect of intrathecal opioids on postoperative nausea and vomiting remains controversial. Although two single-center studies did not find an increase as compared with placebo,^{80,81} a meta-analysis describes a 10 percent increase in the incidence of nausea and a 12 percent increase in the incidence of vomiting.⁸³

Although they are very uncommon with the doses that are currently used, respiratory depression and maternal hypoxemia after cesarean delivery must be considered as potential side effects of intrathecal opioids. The depression of ventilatory responses to hypoxia after 0.3 mg of intrathecal morphine is similar to that associated with equianalgesic

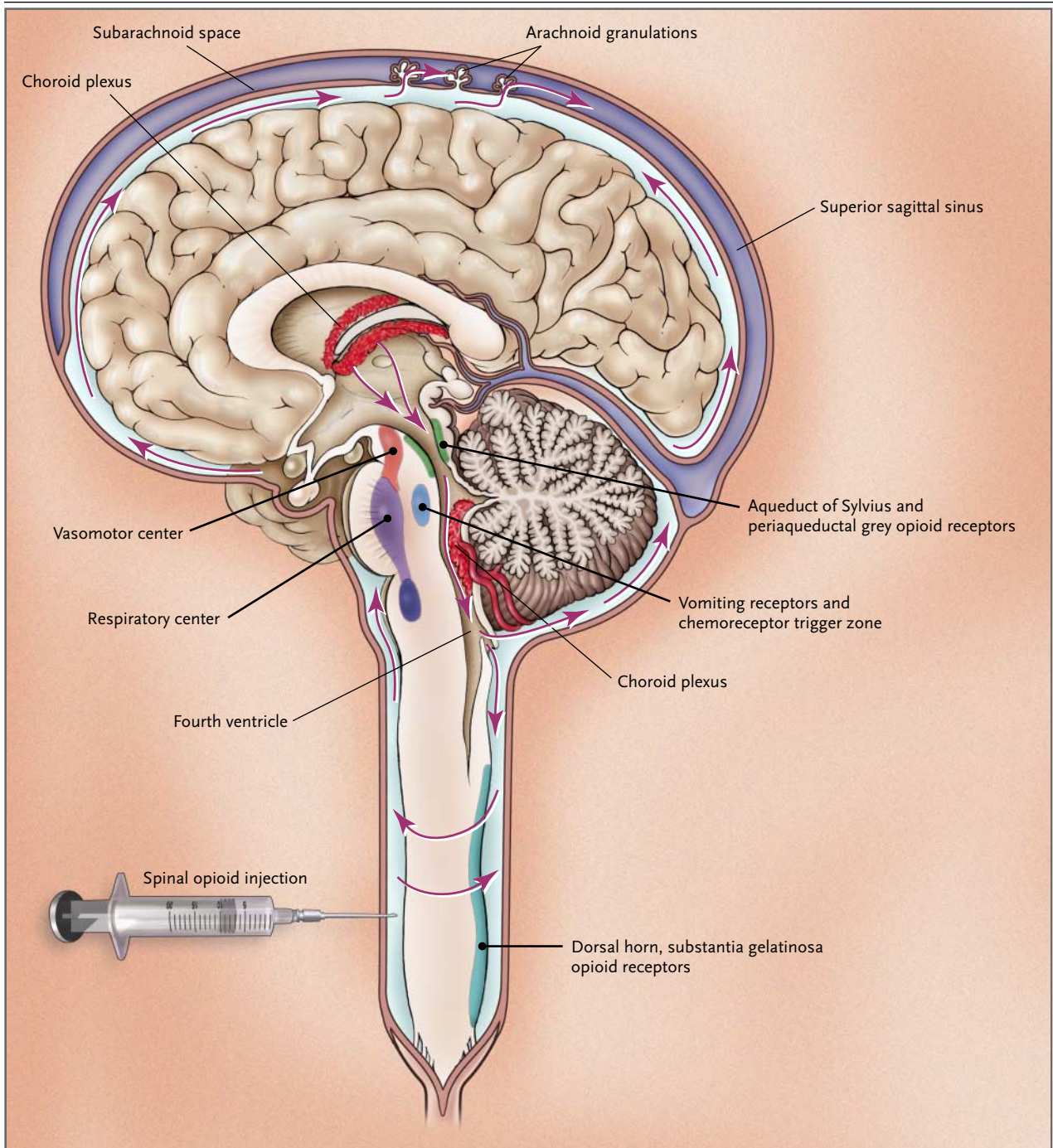


Figure 5. Spread of Opioids in the Cerebrospinal Fluid.

Opioids that are injected into the lumbar intrathecal space exert their analgesic effect by activation of spinal opioid receptors located in the substantia gelatinosa of the dorsal horn. In addition, they can spread upward through the passive flow of cerebrospinal fluid to reach the vasomotor, respiratory, and vomiting centers of the brain. The rostral spread of intrathecal opioids is thought to be responsible for unwanted effects such as respiratory depression, pruritus, hypotension, nausea, and vomiting. Systemic absorption and redistribution to the brain is an alternative route for activating brain-stem opioid receptors that may account for early side effects, whereas rostral spread within the cerebrospinal fluid may be responsible for late side effects.

doses of intravenous morphine but lasts longer.⁸⁴ Parturient women who are thought to be at particular risk for respiratory depression include those who have received previous parenteral opioids, those who are obese, and those who have sleep apnea. Postoperative monitoring of the respiratory rate or hemoglobin oxygen saturation for at least 18 hours after the intrathecal administration of morphine should be considered, so that severe maternal hypoxemia may be avoided.

CONCLUSIONS

In 2002, the American College of Obstetricians and Gynecologists and the American Society of Anesthesiologists issued a joint statement indicating that

a woman's request for pain relief is sufficient medical indication for its use.⁸⁵ Our opinion is that epidural analgesia is a safe, widely used, effective means of pain relief during labor and cesarean delivery. Nonetheless, many questions remain to be answered, and side effects of pharmacologic pain relief during labor continue to be a matter of concern. Labor is a complex and highly individual process; not every woman wants or needs analgesic interventions for delivery. Prenatal education, whenever possible, is the best option for helping women to make an informed decision. The decision to receive any form of analgesia is personal and should be made by the patient in consultation with her obstetrical care provider and anesthesiologist.

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