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Analgesia and Anesthesia in Labor

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Although management of pain in labor is an integral part of modern obstetrics, it is astonishing to realize that obstetric anesthesia has been used for less than 160 years. This article reviews the various pharmacologic and nonpharmacologic options for obstetric pain management in the United States, including efficacy, benefits, and risks. For the purposes of this article, analgesia refers to reduction of pain, whereas anesthesia refers to reduced sensation, or feeling.

History

A brief history of pain management in labor enhances the understanding of current practices. Before the 1800s, anesthesia for medical procedures, including surgery, was not yet available. By the 1840s, however, American physicians had discovered the anesthetic properties of nitrous oxide and ether, publishing these agents' uses in surgical and dental procedures [1]. It was obstetricians in Britain, however, that first identified the use of anesthetics for labor.

Two physicians are generally credited with being pioneers in this area. Dr. John Snow, a prominent general practitioner, published a treatise in 1847 titled ''The Inhalation of the Vapor of Ether,'' which outlined the clinical signs of ether inhalation [2]. A meticulous researcher with a keenly observant eye, Snow thoroughly documented his experience with inhalational anesthetics, both clinically and in the laboratory, measuring various chemical properties of different

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agents. Snow's documentation was so thorough that his guidelines essentially established the standard of care for inhalational anesthesia. Dr. James Young Simpson, a charismatic, highly prominent obstetrician quickly recognized that anesthesia has obstetric uses, and published three case reports of his successful application to laboring women [3,4].

Simpson was soundly criticized for his actions and views, with detractors arguing against such inappropriate use of anesthesia, claiming that it violated God's decree that woman shall toil in labor, and was an unnecessary and possibly dangerous adjunct for labor [1,5,6]. In fact, as recently as 2002 and updated in 2004, the American College of Obstetricians and Gynecologists released a committee opinion stating maternal request for pain relief in labor was sufficient grounds for analgesia, with no other medical conditions required first [7].

Despite the opposition, Snow and Simpson continued to use anesthesia during labor, with chloroform gradually replacing ether as the agent of choice. Proponents of obstetric anesthesia were aided in their efforts when Snow applied anesthesia in 1853 to none other than Queen Victoria herself. Back in the United States, Fanny Longfellow, a prominent woman of society and wife of the poet Henry Wadsworth Longfellow, also availed herself of the opportunity for labor anesthesia, courtesy of Dr. Nathan Keep [8,9]. Whether the use of anesthesia was driven by patient demand or increased availability as more and more doctors were willing to administer it, one thing was clear: by the 1850s, anesthesia for childbirth was here to stay.

In July, 1900, Dr. Oscar Kreis, from Switzerland, administered spinal cocaine to six patients in the second stage of labor, the first documented case of regional anesthesia in obstetrics. Two years later, in 1902, Dr. Hopkins performed the first cesarean delivery in the United States using spinal anesthesia [10], 75 years after the first successful cesarean deliveries had been performed in the United States [11]. Finally, in 1931 a Romanian physician working in Paris, Dr. Eugen Aburel, presented publicly his successful use of epidural analgesia for a patient throughout her labor, the first such application in obstetrics [12]. Patients for the first time had a full complement of techniques available to alleviate the pain of both labor and delivery.

Physiology and anatomy

Uterine innervation stems from a variety of sources. Parasympathetic nerves stemming from S2 to S4 conglomerate into the cervical ganglion of Frankenhäuser. Sympathetic nerves, the predominant influence in uterine innervation, descend from T7 to T8 to the internal iliac plexi bilaterally to meet their parasympathetic counterparts. Together these nerves innervate not only the uterus, but bladder and upper vagina. Within the uterus, nerves terminate both within muscle fibers and the endometrium itself. The perineum is innervated by the pudendal nerve, which also enters the spinal cord at the S2 to S4 levels.

Although these systems are primarily responsible for the function of the uterus, the perception of pain stems from different sites. Visceral afferent fibers from the uterine corpus transmit pain signals to the brain by entering the spinal cord at the T11 and T12 levels, whereas spinal cord levels S2 to S4 receive signals from the cervix, vagina, and perineum. Recognition of this divergence is the key: because of the pain fibers' high entry point in the spinal cord, sacral blockade alone is insufficient to achieve adequate analgesia and anesthesia, particularly in the first stage of labor.

Nonpharmacologic interventions

Before the advent of anesthetic and analgesic medicines, various techniques were used to alleviate the pain of childbirth. Clearly, these measures were implemented without any previous research determining their effectiveness. Today, with multiple medications at clinicians' disposal, alternative therapies are still used for a number of reasons. First, very few if any adverse effects have been demonstrated for the fetus or neonate or parturient with these techniques. Second, many of these techniques are low-cost, and require minimal, if any equipment, making them available when other resources, such as 24-hour epidural availability, are limited or medical indications preclude their use. Finally, many women seek alternative therapies so as to be a more active participant in the labor process. Rather than passively being given drugs, women must take a more participatory approach to the implementation of pain reduction with these methods. This relative empowerment makes nonpharmacologic techniques more attractive for those who wish to experience a ''natural'' childbirth.

Alternative methods' primary disadvantage is their lack of demonstrated efficacy in relieving pain in comparison with medications. One of the difficulties that has hindered alternative pain remedies' acceptance into mainstream obstetrics has been lack of adequate research to determine their use. Part of this stems from confusion regarding differences in end point definitions. What is the end point being measured: reduction of pain? Reduction of need for additional pain interventions? A decrease in cesarean section or operative vaginal delivery rates? Maternal satisfaction with the method? With these thoughts in mind, some of the more common alternative strategies used are discussed next.

Acupuncture

Acupuncture consists of the insertion of fine needles, usually 30- to 32-gauge, into particular sites on the body. These sites are determined based on the presence of meridians, nonanatomic lines of energy coursing through the human body. By altering the energy (often referred to as ''chi''), pain relief can be achieved.

One randomized-controlled trial studied acupuncture versus no acupuncture, with primary outcomes being maternal satisfaction and need for additional analgesia [13]. The acupuncture group required less additional analgesia, but

maternal satisfaction was the same in both groups. There were no differences in length of labor, need for labor augmentation, or operative delivery rates. A second study from Norway also reported similar findings [14]. Both studies, although randomized, were not blinded for obvious reasons. Skilnand et al [15] conducted a randomized-controlled trial using real and sham acupuncture (eg, needles not placed on the classic meridian sites, presumed to have no effect). Pain as assessed by a visual analog scale was significantly reduced in the treatment group both before and after birth, as was need for pharmaceutical analgesia. Gentz [16] reviewed a number of earlier studies performed in the United States and abroad that demonstrated inconsistent or ineffective pain relief. Moreover, all these studies were hampered in their methodology by being uncontrolled and nonrandomized.

Acupuncture studies are difficult to evaluate for a number of reasons. Training levels of acupuncturists varied from a 4-day course [13] to completion of training in a school of acupuncture [15]. There was no uniformity in sites selected for needle placement or number of needles used. Neonatal outcomes were documented in some studies [14] but not others [15].

Massage

Massage has the distinct advantage of being able to be performed by anyone at any time with minimal cost, making it a viable option in almost any circumstance. Standardizing technique to assess effectiveness, however, again proves to be difficult, and very few studies have been conducted to measure its use in labor. Although two studies [17,18] reported a reduction in pain in patients receiving massage during labor, neither study was randomized, and no information on use of other palliative measures was given. In addition, subjects were recruited from a Lamaze class for one study [18], introducing its own set of patient selection biases. No adverse effects were reported. It is impossible from these studies to draw any conclusions regarding massage's effectiveness in labor.

Intracutaneous sterile water blocks

Intracutaneous water blocks involve the injection of 0.05 to 0.1 mL of sterile water using a tuberculin syringe into the sacral area. Four sites are identified: two over the posterior superior iliac spines, and two located 3 cm inferior and 1 cm medial to the first two. The mechanism of action is unknown. Current theories include counterirritation, [19,20], inhibition of pain transmission by nerves, or stimulation of endorphin production [21].

One study [21] randomized women to receive either intracutaneous sterile water blocks or intracutaneous isotonic saline at the same injection sites. Although patient perception of pain was decreased as documented by a visual analog scale, there were no differences in narcotics or epidural use between groups. Similar results were found by Trolle et al [22], which also demonstrated a reduction in cesarean delivery rate (11.4% versus 4.2%; $P < .05$). Martensson

and Wallin [23] altered the study design by randomizing groups to receive sterile water intradermally, sterile water subcutaneously, or saline subcutaneously, the latter serving as the placebo group. Parturients reported lower pain scores by visual analog scale with sterile water injections, regardless of depth compared with the isotonic saline group. No comment was made, however, on use of other analgesics. Finally, Labrecque et al [24] sought to compare sterile water injections with transcutaneous electric nerve stimulation and standard care. Again, pain intensity scores were lower in the sterile water group, and again there were no differences between groups in uses of additional analgesic measures. No adverse effects were reported in any of the studies.

In sum, intracutaneous sterile water blocks may have some use in relieving labor pain; it should be emphasized, however, that this particular technique is used for severe back pain only, and has not been demonstrated to impact any labor pain experienced in the abdominal region.

Water immersion

Spending part or most of labor immersed in water has been promoted by various groups and popularized in the press. Some hospitals have even installed birthing tubs for their patients to use. A quality review of this modality can be found elsewhere [25]. Observational, cohort, and randomized-controlled trials have all produced conflicting reports on the efficacy of water immersion in relieving labor pain. In addition, controversies exist over proper water temperature, time the patient should spend in the water, and whether it should be permitted in the presence of ruptured membranes. No definitive conclusions can be drawn. Ironically, this intervention can be quite costly, because substantial expense is required to install tubs and maintain water temperature and quality. Monitoring the fetus is not possible with the parturient's abdomen submerged, making this a potentially unacceptable therapy for a complicated pregnancy.

Other modalities

Additional therapies studies including biofeedback, hypnosis, respiratory autogenic training, aromatherapy, music therapy, and audio-analgesia have been reviewed and critiqued [26,27], with too little data to formulate any conclusions.

Intravenous analgesia

Intravenous analgesia was introduced in the mid 1850s as an alternative to inhalational anesthesia for labor. These agents, which are opioid derivatives, are still commonly used, particularly in the earlier stages of labor and where regional anesthesia is not available. A key concept to be understood is that intravenous analgesia can reduce but not eliminate the pain of labor, and even the most commonly used agents achieve moderate success at best. Soontrapa et al [28] deter-

mined that less than 25% of patients administered an intravenous opioid got adequate relief, whereas Olofsson et al [29] found that no substantial effect occurred, with maternal sedation being mistakenly interpreted as pain relief. Medications used fall in two main categories: pure opioid agonists and opioid agonist-antagonists. The most commonly used drugs during labor are discussed next.

Morphine

Morphine was the first pure opioid administered for labor analgesia, with the usual dose ranging from 1 to 4 mg. The peak effect occurs 20 minutes after intravenous administration, and 1 to 2 hours if given intramuscularly. Duration of action is 4 to 6 hours. Morphine rapidly crosses the placental barrier and can cause significant neonate respiratory depression. Besides neonatal effects, maternal side effects include respiratory depression, sedation, nausea, emesis, and dizziness. Because of its prolonged half-life, strong sedation, and neonatal effects, morphine is rarely used for labor in the United States.

Meperidine (Demerol)

Meperidine, introduced into obstetrics in the 1940s, is the most commonly used opioid for pain relief in labor [30]. Typical doses are 50 to 100 mg intramuscularly or 25 to 50 mg intravenously. Its onset of action is approximately 10 minutes for intravenous and 50 minutes for intramuscular administration. Duration of action is approximately 4 hours. Meperidine can also produce neonatal respiratory depression, with the severity of effect determined by dose administered and time from dosing to delivery. A neonate is most likely to show effects of meperidine administration if delivered 2 to 3 hours after the medicine is given. Alternatively, the neonate is less likely to be affected if delivered less than 1 hour after dosing (before onset of action) or more than 4 hours after dosing (past duration of action).

Meperidine is preferred over morphine because of its quicker onset and shorter duration. In addition, neonates seem to be less sensitive to meperidine than morphine's respiratory effects [31]. A large disadvantage is that meperidine is metabolized to normeperidine in the neonate, which has a substantially longer half-life. Repeated doses can lead to an accumulation of opioid within the neonate that persists after delivery. Because of this, and the availability of alternative medications, meperidine is not on formulary for labor analgesia at Johns Hopkins Hospital.

Fentanyl

Fentanyl is a synthetic opioid with some distinct advantages over morphine and meperidine. Its onset of action is rapid (2–3 minutes administered intravenously), and duration of action is about 60 minutes. Usual dosages are 50 to 100 μg intramuscularly, or 25 to 50 μg intravenously. Fentanyl does cross the

placenta [32], although not as readily as morphine or meperidine [33,34]. Some studies have suggested fentanyl does not alter neonatal Apgar scores or umbilical cord blood gases, although neonatal respiratory depression has been identified as a possible side effect. Fentanyl's main improvement over its predecessors is decreased maternal sedation and nausea [35], and decreased transport to the fetal system. Side effects can be similar to other opioids and include constipation, dry mouth, and urinary retention. Pruritus does not seem to be as much an issue as with morphine or meperidine. Fentanyl has been shown to decrease temporarily beat-to-beat variability in fetal heart tracings and occasionally trigger a benign sinusoidal wavelike pattern within 30 minutes of administration [36].

Opioid agonist-antagonists were developed in the hopes of limiting the maternal and neonatal respiratory depression seen with pure opioids. Butorphanol can be given intravenously (1–2 mg) or intramuscularly (2–4 mg). The peak effect occurs in 4 to 5 minutes with intravenous dosing, and 30 to 60 minutes given intramuscularly. Duration of action with either route is 3 to 4 hours. The typical dose of nalbuphine is 10 mg intramuscularly or intravenously. The peak effect is 2 to 3 minutes intravenously and less than 15 minutes when given intramuscularly. Duration of action is 3 to 6 hours regardless of route.

At standard doses, both butorphanol and nalbuphine can cause maternal respiratory depression equivalent to that of a standard dose of morphine. Although increasing doses of morphine has an increasing effect on depression, butorphanol and nalbuphine have a "ceiling effect," which limits their impact on maternal respiratory drive with increasing doses. Both agents can cause neonatal respiratory depression, and neither has been shown to be more efficacious than the agents previously mentioned. Like its pure opioid counterparts, nalbuphine does have an effect on fetal heart rate tracings, leading to decreased accelerations and variability [37].

Caution must be exercised in using these in patients who are on chronic narcotics for other conditions or are drug abusers, because butorphanol and nalbuphine's antagonist effect can precipitate an acute withdrawal. A summary of the most commonly used medications can be found in Table 1.

Table 1
Commonly used medications

Drug	Dose	Onset of action	Duration
Morphine	1–2 mg IV 5–10 mg IM	20 min IV 1–2 h IM	4–6 h
Meperidine	25–50 mg IV 50–100 mg IM	10 min IV 50 min IM	4 h
Fentanyl	25–50 μg IV 50–100 μg IM	2–3 min IV 7–8 min IM	1 h
Butorphanol	1–2 mg IV 2–4 mg IM	4–5 min IV 30–60 min IM	3–4 h
Nalbuphine	10 mg IV or IM	2–3 min IV <15 min IM	3–6 h

Abbreviations: IM, intramuscularly; IV, intravenously.

To reduce the amount of opioid needed for analgesia, combinations of medicines with opioids have been tried. Sedatives, such as barbiturates, are based on the premise that reducing maternal anxiety may reduce the perception of pain. Not only do barbiturates have no analgesic properties, their long half-lives and crossing of the placenta make them ineffective and potentially harmful for the neonate. Benzodiazepines have shorter half-lives, but their effect on neonates can be just as dramatic. Both agents can potentiate maternal respiratory depression. For these reasons, sedatives are not recommended for use during labor.

Antiemetics

Promethazine (Phenergan), a phenothiazine derivative, is frequently used in conjunction with an analgesic. Its primary advantages are that it can treat the nausea associated with opioids and provide some sedation for maternal anxiety without suppressing maternal respiratory drive. Promethazine does cross the placenta, but has not been shown to have adverse effects on the neonate.

Hydroxyzine (Vistaril), an H_1 antagonist, has the advantage of treating pruritus in addition to being an antiemetic and mild sedative. It can only be given intramuscularly and orally, because no intravenous preparations are available.

Paracervical block

Paracervical block consists of the administration of a local anesthetic on either side of the cervix where the afferent fibers of the nerves are located. First described in 1945, paracervical block was commonly used throughout the 1950s. Agents used include 1% lidocaine with or without epinephrine, or bupivacaine, the former more common in the United States, with the latter more common in Europe.

Paracervical block's primary advantage is its availability, requiring only local anesthetic, a spinal needle, and an obstetrician's expertise. Its greatest drawback is the incidence of fetal bradycardia following its administration, a side effect brought to light in the early 1960s that continues to be paracervical block's biggest disadvantage. Although the bradycardia can be of short duration and no clinical consequence, it can also be prolonged and lead to severe adverse outcomes including perinatal death. This bradycardic effect is not uncommon. Thought initially to occur approximately 70% of the time [38], recent estimates with current techniques put its occurrence at 15% [39].

The reason for the fetal bradycardia is unclear, with multiple theories suggested, including direct injection of anesthetic into the fetal head, vasoconstriction of the uterine artery [38], use of epinephrine to prolong the anesthetic's effect, and pressure on the fetal head [39]. Levy et al [40] found no differences in umbilical artery pH in neonates whose mothers received paracervical block as compared with other methods. In this study, epinephrine was not used, and the incidence of fetal bradycardia was not commented on. Similarly, Kaita et al [41]

detected no differences in fetal oxygen saturation when either paracervical block or epidural anesthesia was used, so the mechanism behind the bradycardia has yet to be determined.

Because of the possibility of bradycardia, paracervical block is not recommended in the presence of a nonreassuring fetal heart tracing, thereby limiting its applicability. The duration of action using lidocaine is approximately 20 to 40 minutes. Lidocaine toxicity can occur, so aspiration before injection to confirm the needle is not intravascular and monitoring the total amount of lidocaine given is essential. Degree of pain relief offered by a paracervical block is not well studied.

Regional anesthesia

It could be argued that the most dramatic change in obstetric practice has been the use of regional anesthesia. Since its introduction in the early part of the twentieth century, regional anesthesia has rapidly gained widespread acceptance. Rates of epidural use vary widely, and are as high as 98% in some European countries [42]. In the United States, epidural rates have been estimated as high as 50% [43]. Rates can vary, however, depending on multiple factors, including availability of anesthesia services; criteria for use (stage of labor versus on demand); and even size of hospital [43,44]. Within the same region, individual hospitals can differ substantially in rates [45], indicating other factors at work, such as whether the patient's labor was induced or spontaneous [46].

Although regional anesthesia and epidural are terms used interchangeably, the latter is merely a subset of the former. Epidural involves administration of an analgesic or anesthetic in the space around the dura mater surrounding the spinal cord. Spinal anesthesia requires penetration of the dura into the cerebrospinal fluid–filled cavity in which the spinal cord sits (Fig. 1). Puncture of the dura (wet tap) during administration can lead to a tiny amount of spinal fluid leaking into the epidural space. The concomitant decrease in cerebrospinal fluid can lead to a postdural headache. Small amounts of drug are needed to produce substantial anesthesia for a spinal, whereas relatively large amounts are needed to produce a systemic effect when placed epidurally. Recently, anesthesiologists have used a combined spinal and epidural technique, taking advantage of spinal anesthesia's rapid onset of action with the ability to administer an epidural for a prolonged period of time.

The epidural space was traditionally considered continuous from the foramen magnum to the sacral hiatus; however, studies performed in the late 1980s demonstrated the presence of connective tissue bands that form septa within the space [47–49]. These observations may help explain the presence of windows or unanesthetized unilateral areas despite proper epidural placement.

Medications used for epidural placement include analgesics (opioids); anesthetics; or a combination. Opioids and anesthetics are commonly used in combination, because the two together seem to have a synergistic effect [50–52].

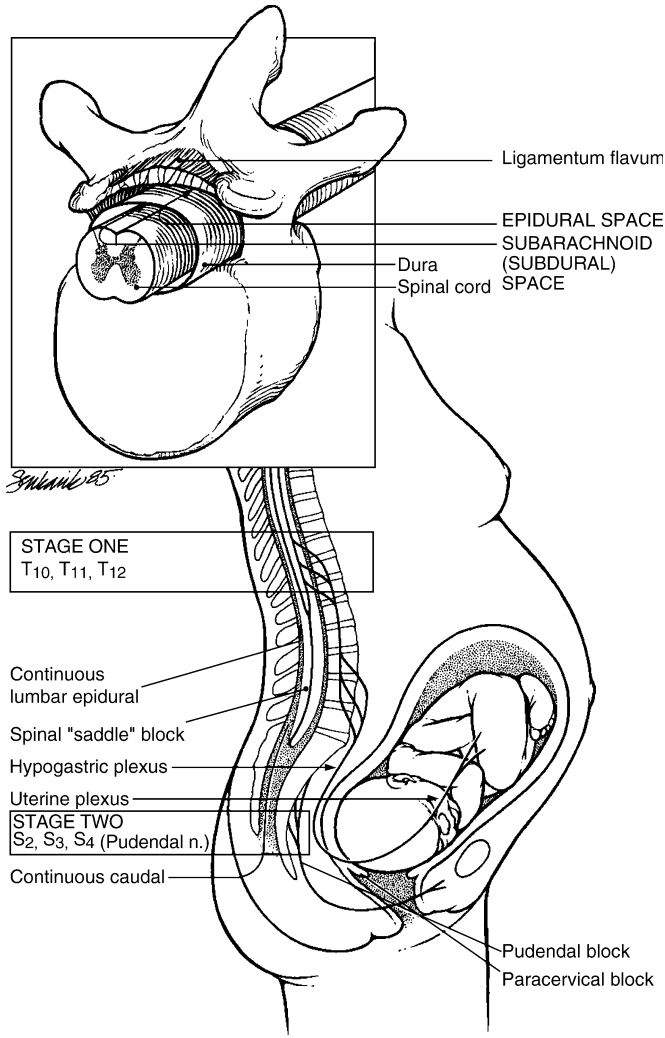

Fig. 1. Spinal anatomy for obstetric anesthesia. (*From* Gabbe SG. Obstetrics: normal and problem pregnancies. 4th edition. Philadelphia (PA): Churchill Livingstone; 2002. Figure 15-1; with permission.)

Epinephrine is commonly added to the analgesic, because it lessens the amount needed for adequate pain relief, and has been shown to reduce maternal sedation [53–55].

Morphine was the first opioid used for epidural analgesia, but its long onset time and moderate efficacy made it less than ideal. Meperidine has also been used, but concerns over its side effects, including risk of seizures, have diminished its appeal. The newer opioids fentanyl and sufentanil, discussed previously, are better tolerated.

More commonly used for epidural block are the local anesthetics, which obviate the concern for neonate respiratory depression that surrounds any maternal opioid administration. All of the local anesthetics are derivatives of cocaine, with differences in onset of action, duration, and side effect profiles distinguishing among them.

Bupivacaine is a frequently used local anesthetic for epidural anesthesia because of its long duration of action, low placental transfer, and good effect both in early and late stages of labor [56]. It's most serious side effect, however, is that of cardiotoxicity, particularly if the catheter has been inadvertently placed intravenously or in the subarachnoid space. Pregnant patients seem to be more susceptible to this adverse effect than nonparturients, with a variety of physiologic changes of pregnancy proposed as the reasons [57,58]. To prevent this, anesthesiologists routinely administer a small amount (test dose) of the drug on initial catheter insertion to confirm proper placement and monitor closely for adverse effects.

Lidocaine is another agent used in obstetrics. Its shorter duration of action and less effective pain relief when compared with bupivacaine makes it less used. Lidocaine's major advantage over bupivacaine, however, is its much lower risk of cardiotoxicity.

Ropivacaine, one of the new anesthetics, is similar to bupivacaine in its structure and potency, but seems to have a more rapid clearance, providing a larger margin of safety against cardiotoxicity.

Common side effects of regional anesthesia include pruritus, inability to void, and hypotension. All are easily managed, with the last frequently addressed by administering to the patient a fluid bolus of 500 to 1000 mL of fluid before epidural placement. An excellent analysis of epidural anesthesia's side effects and their management is provided by Mayberry et al [59].

More important is regional anesthesia's effect on labor itself. Despite claims to the contrary, epidural anesthesia has not been found to increase the rate of primary cesarean section [60,61]; however, it does seem to increase the rate of oxytocin administration [61], operative vaginal delivery [60,61], episiotomy [62,63], and antibiotic use because of fever [64]. In addition, epidural anesthesia has been shown to increase the length of both the first and second stages of labor because the cervix may dilate more slowly than suggested by the Friedman curve [61,65].

Because it dramatically changes the degree of medical intervention and maternal-fetal surveillance required, epidural and spinal anesthesia have garnered both advocates and opponents to its use. A number of alterations in childbirth outcomes have been attributed to epidural anesthesia, ranging from improved maternal respiratory function [66] to impaired breastfeeding [67].

Summary

Whether given as an epidural, spinal, or combination, regional anesthesia is an integral part of obstetrics in the United States. A variety of drugs and dosages

are used in various combinations, with no one protocol exceeding others in terms of efficacy and safety.

The availability of anesthesia and analgesia has had an extraordinary impact on the field of obstetrics in the twentieth century. Knowledge of the techniques and medications used, their potential toxicities, and effects on the labor process itself can only enhance obstetricians' management of the parturient in labor.

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