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# Evidence-Based Obstetric Anesthesia: An Update on Anesthesia for Cesarean Delivery

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## 1. Introduction

Severe hemorrhage and infection causing significant morbidity and mortality limited the use of cesarean section until the twentieth century, when important advances in aseptic, surgical, and anesthetic techniques improved the safety of this procedure for both woman and fetus [1-3].

The most common indications for cesarean delivery include dystocia, prior cesarean delivery, malpresentation, multiple gestation, fetal distress (nonreassuring fetal status), and maternal request [1-3]. Since late 70's, a progressive increase in the cesarean delivery rates has been observed worldwide and several factors are associated with this finding: maternal, obstetric, fetal, medicolegal, and social factors are pivotal for this increment. Actually, cesarean delivery rates have increased to around 30% in the last decade [1-3]. Notably, cesarean delivery rates are likely to increase further as women are requesting an elective cesarean delivery even for their first baby. Although controversial, the American College of Obstetricians and Gynecologists (ACOG) has suggested that it is ethical for an obstetrician to perform an elective cesarean delivery if the physician believes that the cesarean delivery promotes the health of the mother and fetus more than a vaginal delivery.

The selection of regional or general anesthesia for cesarean delivery depends on the experience of the anesthesiologist, past medical history of the patient, indications and urgency of the cesarean delivery, maternal status, and desires of the patient. Past medical, surgical, and obstetric history, presence or absence of labor, and available resources should also be considered by the anesthesiologist [4-6]. Considering these issues, the main aims of this chapter are to discuss the most important topics involved in anesthesia for cesarean delivery and the most recent scientific evidences regarding techniques and perioperative management of obstetric patients. We emphasize that this chapter is only a brief review

focusing on main issues involved in anesthesia for cesarean delivery and more comprehensive reviews and recommendations are available elsewhere [4-6].

## **2. Perianesthetic evaluation of the obstetric patient**

### **2.1 Preanesthetic evaluation**

All women admitted for labor and delivery are potential candidates for the emergency administration of anesthesia. Considering this fact, the anesthesiologist ideally should evaluate every patient shortly after admission. The anesthesiologist should conduct a focused history and physical examination before providing anesthesia care. This should include, but should be not limited to, a maternal health and anesthetic history, a relevant obstetric history, a baseline blood pressure measurement, allergies, and performance of an airway, heart, and lung examination [7]. When a neuraxial anesthetic is planned, the patient's back should also be examined. Ideally, for high-risk women, preanesthetic evaluation should occur in the late second or early third trimester. This practice offers the opportunity to provide women with information, solicit further consultations, optimize medical conditions, and discuss plans and preparations for the upcoming delivery, perhaps in a multidisciplinary basis [8,9]. In some cases, the urgency or emergency of the situation allows limited time for evaluation before induction of anesthesia. Nevertheless, essential information must be obtained, and risks and benefits of anesthetic management decisions should be discussed on a case-by-case basis.

Usually, obtaining an informed consent is strongly recommended [10]. The ethical issues in obtaining consent from the obstetric patient can be challenging considering the potential clinical situations, such as the pain and stress of labor and sudden changes in maternal and fetal status, sometimes requiring emergency care. Nevertheless, there is general consensus that pregnant women appear to want more rather than less information regarding the risks of anesthetic interventions during a preanesthetic evaluation. Women usually should be aware of the following neuraxial anesthetic risks: the possibility of intraoperative discomfort and a failed/partial blockade, the potential need to convert to general anesthesia, the presence of weak legs, hypotension episodes associated to discomfort, and the occurrence of an unintentional dural puncture (whenever an epidural technique was used) [11]. Backache and urinary retention could be considered for discussion, but the risk for paraplegia should not to be routinely addressed unless the patient specifically asked about it [11]. Finally, and most important, anesthesiologists are encouraged to discussion of anesthetic risks and techniques and use informed consent as an opportunity to establish a closer patient-physician relationship rather than a simple tool to avoid litigation.

### **2.2 Fasting recommendations and aspiration prophylaxis**

Although there is a lack of data regarding the relationship between recent food intake and subsequent aspiration pneumonitis, the patient should be always asked about oral intake and fasting period. Gastric emptying of clear liquids during pregnancy probably occurs relatively quickly since the residual content of the stomach does not appear to be different from baseline fasting levels in nonlaboring pregnant women [12,13]. The uncomplicated patient undergoing elective cesarean delivery may drink modest amounts of clear liquids (water, fruit juices without pulp, clear tea, etc) up to 2 hours before induction of anesthesia

[6]. The volume of liquid ingested is less important than the absence of particulate matter. Women with additional risk factors for aspiration (e.g., morbid obesity, diabetes, difficult airway), or laboring women at increased risk for cesarean delivery may have further restrictions of oral intake [6]. Routinely, ingestion of solid foods should be avoided during labor and in women undergoing elective cesarean delivery. A fasting period for solids of 6 to 8 hours is still recommended [6].

In women scheduled to cesarean section and considered to be in high-risk for aspiration, a pharmacological prophylaxis should be considered if time permits. The literature does not sufficiently examine the relationship between reduced gastric acidity and the frequency of emesis, pulmonary aspiration, morbidity, or mortality in obstetric patients who have aspirated gastric contents. Evidence supports the efficacy of preoperative nonparticulate antacids (0.3 M sodium citrate) in decreasing gastric acidity during the peripartum period, without affecting gastric volume [14]. Additionally, the literature suggests that H<sub>2</sub> receptor antagonists such as ranitidine or famotidine are effective in decreasing gastric acidity in obstetric patients and supports the efficacy of metoclopramide in reducing peripartum nausea and vomiting [15]. Notably, intravenously administered H<sub>2</sub> receptor antagonists and metoclopramide require at least 30 to 45 minutes to effectively reduce gastric acidity [15]. Proton pump inhibitors such as omeprazole can achieve a higher gastric pH than the H<sub>2</sub> receptor antagonist ranitidine [16], although ranitidine combined with sodium citrate is more cost effective [17].

### **2.3 Equipment and facilities in obstetric anesthesia**

Labor and delivery units may be adjacent to or distant from the operating rooms. Nonetheless, equipment, monitoring material, facilities, and support personnel available in the obstetric operating room should be comparable to those available in the main operating room [6]. In addition, personnel and equipment should also be available to care for obstetric patients recovering from major neuraxial or general anesthesia and postoperative (post-cesarean) recovery unit should be completely equipped as well. Resources for the conduct and support of neuraxial anesthesia and general anesthesia should include those necessary for the basic delivery of anesthesia and airway management as well as those required to manage complications. The immediate availability of these resources is essential, given the frequency and urgency of the anesthesia care provided. Equipment and supplies should be checked on a frequent and regular basis and the necessary drugs, including vasopressors, emergency medications, and drugs used for general and neuraxial anesthesia should be promptly available [6].

Additionally, attention should be given to the availability and accurate functioning of monitors for anesthesia and the management of potential complications (e.g., failed intubation, cardiopulmonary arrest, inadequate analgesia, significant hypotension or bradycardia, respiratory depression, pruritus, vomiting, etc) [6]. Basic monitoring includes maternal pulse oximetry, electrocardiogram (ECG), noninvasive blood pressure monitoring and fetal heart rate (FHR) monitoring. Invasive hemodynamic monitoring should be considered in women with cardiovascular diseases, refractory hypertension, or other specific situations. Bispectral index monitors or other depth of anesthesia monitors have received only limited evaluation in women undergoing cesarean delivery but could be considered in some situations [18].

### 3. Anesthesia for cesarean delivery

#### 3.1 Regional versus general anesthesia: what are the main evidences?

Neuraxial techniques (spinal, epidural, combined spinal-epidural – CSE) are the preferred methods of providing anesthesia for cesarean delivery as compared to general or local anesthesia. Notably, more recently, neuraxial anesthesia is administered to some women who would have received general anesthesia in the past. For example, umbilical cord prolapse, placenta previa, some cardiovascular diseases and severe preeclampsia are no longer considered absolute indications for general anesthesia. Several studies and surveys indicated a progressive increase in the use of neuraxial anesthesia, especially spinal anesthesia, for both elective and emergency cesarean deliveries and similar increases have been observed in both developed and developing countries [19]. Table 1 describes the main factors involved in the process of selection and indication of anesthetic techniques for cesarean delivery.

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#### Regional (neuraxial) versus general anesthesia for cesarean delivery – main indications

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Regional (neuraxial) anesthesia:

- Risk factors for difficult airway or aspiration
- Maternal desire to witness birth and/or avoid general anesthesia
- Improved postoperative analgesia (neuraxial opioids)
- Presence of comorbid conditions
- Reduced fetal drug exposure and blood loss
- Allows presence of husband or support person

General anesthesia:

- Presence of comorbid conditions that contraindicate a neuraxial technique
  - Insufficient time to induce neuraxial anesthesia for urgent delivery
  - Failure of neuraxial technique
  - Maternal refusal or failure to cooperate with neuraxial technique
  - Planned of more complex surgical procedures during cesarean delivery (e.g. ex-utero intrapartum treatment (EXIT) procedure)
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Table 1. Main factors involved in the selection of anesthetic techniques for cesarean delivery

The greater use of neuraxial anesthesia for cesarean delivery has been attributed to several factors, such as the growing use of epidural techniques for labor analgesia, improvement in the quality of neuraxial anesthesia with the addition of an opioid or other adjuvants to the local anesthetic, the risks of airway complications during general anesthesia in obstetric patients, the need for limited neonatal drug transfer, the ability of the mother to remain awake to experience childbirth, presence of a support person in the operating room, lack of experience of the anesthesiologists to provide general anesthesia in the obstetric setting and several others [20-23].

When choosing regional or general anesthesia for cesarean delivery, we should always consider both maternal and neonatal outcomes. Maternal outcome studies have primarily focused on maternal morbidity and mortality, and neonatal outcome studies have focused essentially on umbilical cord pH, Apgar score, the need for ventilatory assistance at birth, and neurobehavioral scores.

Maternal mortality following general anesthesia has been a primary factor for the transition toward greater use of neuraxial anesthesia for cesarean delivery in the last few decades. Notably, maternal outcome seems to be better with regional anesthesia than with general anesthesia. Hawkins and colleagues compared the anesthesia-related maternal mortality rate from 1979 to 1984 with that for the period from 1985 to 1990 in the United States and found that the case-fatality risk ratio for general versus neuraxial anesthesia was as high as 16.7 in the years 1985 to 1990 [24]. The reason for this difference is primarily related to the respiratory system of the parturient since difficult tracheal intubation is 10 times higher in the parturient than in the general population and hypoxemia develops faster during periods of apnea. Of interest, these data may overstate the relative risk of general anesthesia, because this form of anesthesia is used principally when neuraxial anesthetic techniques are contraindicated for medical reasons and/or may reflect the growing acceptance of performing neuraxial techniques in parturients with significant comorbidities [21,22]. Importantly, although general anesthesia is still correlated with higher incidence of maternal deaths as compared to regional anesthesia, a recent report suggests that a significant reduction in general anesthesia-related deaths occurred in the recent years [25].

Of note, airway management experience is decreasing in the obstetric setting. Hawthorne and colleagues found that the incidence of failed tracheal intubation increased from 1 in 250 in 1984 to 1 in 300 in 1994 [26]. In a recent review of maternal mortality causes, Mhyre and colleagues found that "airway problems" is still a leading cause of maternal mortality, but that the problems occurred mostly during emergence or tracheal extubation [27].

Maternal morbidity is also lower with the use of neuraxial anesthesia techniques than with general anesthesia. In a systematic review of controlled trials comparing major maternal and neonatal outcomes with the use of neuraxial anesthesia and general anesthesia for cesarean delivery, Afolabi and colleagues found less maternal blood loss and shivering but more nausea in the neuraxial group [20]. Prospective audits of post-cesarean delivery outcomes have indicated that in the first postoperative week, women who received neuraxial anesthesia had less pain, gastrointestinal stasis, coughing, fever, and depression and were able to breast-feed and ambulate more quickly than women who received general anesthesia [23].

Although neonatal outcome seems to be better when regional anesthesia is used, differences among diverse anesthetic techniques are not so clear. Apgar and neonatal neurobehavioral scores are relatively insensitive measures of neonatal well-being, and umbilical cord blood gas and pH measurements may reflect an obstetric bias (indication for the cesarean delivery rather than differences in anesthetic techniques). Some previous studies have found that umbilical artery pH was greater in the neonate delivered with general anesthesia, but clinical parameters (e.g., Apgar score and the need for assisted ventilation) were better when regional anesthesia was used [28]. The acidemia found following regional anesthesia seems

to be increased after spinal as compared to epidural anesthesia, but has not been related to any clinically significant neonatal complication [20,28].

Therefore, the decision to use a particular anesthetic technique for cesarean delivery should be individualized and based on several factors. These should include anesthetic, obstetric, or fetal risk factors, urgency, the preferences of the patient, and the judgment of the anesthesiologist. Neuraxial techniques are usually recommended and preferred to general anesthesia for most cesarean deliveries. For these reasons, most elective cesarean deliveries are now performed under regional anesthesia [29].

### **3.2 Spinal, epidural, combined spinal-epidural or general anesthesia**

Spinal anesthesia is commonly used rather than epidural anesthesia for elective cesarean delivery because with spinal anesthesia the speed of onset is quicker, the quality of anesthesia is considered to be superior and the failure rate is lower. Riley and colleagues found that spinal anesthesia leads to a more efficient utilization of operating room time than epidural anesthesia because time until skin incision is faster with spinal anesthesia [30]. The most common complication from spinal anesthesia is hypotension, which may explain the decreased umbilical artery pH as compared with both epidural and general anesthesia [31]. The spinal anesthesia is a simple and reliable technique that allows visual confirmation of correct needle placement (by visualization of cerebrospinal fluid leak) and is technically easier to perform than the epidural. Spinal anesthesia provides a rapid onset of dense blockade that is typically more profound than that provided with an epidural technique, resulting in a reduced need for supplemental intravenous analgesics or conversion to general anesthesia [30,32,33]. Considering that a smaller amount of local anesthetic is needed to establish a functional spinal blockade, spinal anesthesia is associated with negligible maternal risk for systemic local anesthetic toxicity and with minimal drug transfer to the fetus, as compared to epidural and general anesthesia [34]. Given these advantages, spinal anesthesia is now the most commonly used anesthetic technique for cesarean delivery worldwide [19,35].

As commonly used for other conventional surgical procedures, the spinal technique should be performed at the L<sub>3</sub> to L<sub>4</sub> interspace or below. These interspaces are used to avoid the potential for spinal cord trauma. Spinal anesthesia is usually administered as a single-injection procedure through a non-cutting, pencil-point needle that is usually 25-gauge or smaller. A number of different needle designs are available and the size and design of the needle tip affect the incidence and severity of post-dural puncture headache (PDPH). For that reason, if spinal anesthesia is chosen, small pencil-point spinal needles should be used instead of larger cutting-bevel spinal needles [36].

Continuous spinal anesthetic technique can be used in some circumstances, especially in the setting of an unintentional dural puncture with an epidural needle. Additionally, intentional continuous spinal anesthesia may also be desirable in certain settings, when the reliability of a spinal technique and the ability to precisely titrate the initiation and duration of anesthesia are recommended (e.g., morbidly obese patients or some cardiovascular diseases). However, technical difficulties, catheter failures, concerns about the risks for neurological complications and a higher incidence of post-dural puncture headache severely restrict this technique from a widespread use [37,38].

The overall use of epidural anesthesia for elective cesarean delivery has decreased, in part because the resulting block is less reliable than that provided by spinal anesthesia. Conversely, the use of epidural anesthesia for nonelective cesarean delivery has increased, primarily as a result of the greater use of epidural analgesia during labor [30]. Although medications used in the spinal and epidural spaces are identical, epidural local anesthetic and opioid doses are up to 10 times greater than doses given spinally leading to concerns regarding toxicity and efficacy. Contrariwise, advantages of the epidural technique include a slower onset of sympathetic blockade, which may allow compensatory mechanisms to attenuate the severity of hypotension episodes [30]. Furthermore, a catheter-based technique also allows titration of the level and duration of anesthesia and continuous post-cesarean delivery analgesia.

The CSE technique incorporates the rapid and predictable onset of a spinal blockade with the ability to augment anesthesia by injection of additional drug through the epidural catheter [39-41]. In 1981, Brownridge [39] reported the first use of the CSE technique for cesarean delivery through separate spinal and epidural needles introduced at different interspaces. Carrie and O'Sullivan [40] subsequently reported the needle-through-needle technique via a single interspace for cesarean delivery, which has become the most popular technique. More recently, Davies and colleagues compared CSE with epidural anesthesia alone for elective cesarean delivery and reported more rapid onset, greater motor blockade, and lower pain scores at delivery in the CSE group [41]. The main disadvantages of CSE techniques are an untested epidural catheter and hypotension [42]. Additionally, the CSE technique is certainly more time-consuming as compared to spinal anesthesia only.

An alternative CSE technique is the extradural volume extension (EVE) technique [43-45]. In this technique, spinal administration of a small dose of local anesthetic is followed by the administration of saline through the epidural catheter. Although there were conflicting findings, this technique has been related to a higher rostral spread of the blockade [43-45].

Table 2 demonstrates the main differences regarding the various neuraxial anesthetic techniques for cesarean delivery. With all neuraxial techniques, an adequate sensory level of anesthesia is essential to minimize maternal pain and avoid the urgent need for administration of general anesthesia. Because motor nerve fibers are typically larger and more difficult to block, the complete absence of hip flexion and ankle dorsiflexion most likely indicates that a functional sensory and sympathetic block is also present in a similar (primarily lumbosacral) distribution. However, because afferent nerves innervating abdominal and pelvic organs accompany sympathetic fibers that ascend and descend in the sympathetic trunk ( $T_5$  to  $L_1$ ), a sensory block that extends rostrally from the sacral dermatomes to  $T_4$  should be the goal for cesarean delivery anesthesia [46-48]. The majority of anesthesiologists use the absence of cold temperature sensation to a  $T_4$  level to indicate an adequate blockade height for cesarean delivery [46-48]. Alternatively, a  $T_6$  blockade to touch may provide a pain-free cesarean delivery for most parturients and could be used as a reference. Because the undersurface of the diaphragm ( $C_3$  to  $C_5$ ) and the vagus nerve may be stimulated by surgical manipulation during cesarean delivery [49], maternal discomfort and other symptoms, particularly nausea and vomiting may occur despite a  $T_4$  level of blockade. The use of systemic and especially neuraxial opioids are effective in preventing or alleviating these symptoms [49,50].



Technique	Advantages	Disadvantages
Spinal anesthesia	Technically simple Rapid onset and dense blockade Low doses of local anesthetic required	Limited duration Limited level block titration Increased incidence of hypotension
Epidural anesthesia	No dural puncture is required Ability to titrate extent of sensory blockade Continuous perioperative anesthesia	Slow onset of surgical anesthesia Higher incidence of failure High doses of local anesthetic required
CSE* anesthesia	Low doses of local anesthetic and opioid Rapid onset and dense blockade Ability to titrate extent of sensory blockade Continuous perioperative anesthesia	Delayed verification of functioning epidural catheter Technique slightly more difficult Time consuming

\*CSE = Combined spinal-epidural anesthesia.

Table 2. Main advantages and disadvantages regarding type of neuraxial anesthesia for Cesarean Delivery

The choice of local anesthetic agent (and adjuvants) used to provide spinal anesthesia depends on the expected duration of the surgery, the postoperative analgesia plan, and the preferences of the anesthesiologists. For cesarean delivery, the local anesthetic agent of choice is typically bupivacaine since its spinal administration usually results in a dense block of long duration. However, several different doses of bupivacaine have been described in the literature and the dose of spinal bupivacaine that has been successfully used for cesarean delivery ranges from 4.5 to 15 mg [40,46,49]. In general, pregnant women require smaller doses of spinal local anesthetic as compared to nonpregnant women. Reasons include a smaller CSF volume in pregnancy, rostral movement of hyperbaric local anesthetic in the supine pregnant patient, and the greater sensitivity of nerve fibers to the local anesthetic during pregnancy [51]. Overall, the mass of local anesthetic, rather than the concentration or volume, is thought to influence the spread of the resulting blockade [52]. However, the specific influence of the dose and baricity on the efficacy of the block is somewhat controversial and may be influenced by other factors, such as co-administration of neuraxial opioids.

More recent data suggest that lower anesthetic doses can be used, although there is some controversy regarding recommendations. The anesthesiologist should consider whether adjuvant drugs will be used and whether the risks of giving supplemental analgesia or conversion to general anesthesia that are associated with low doses of bupivacaine outweigh the potential benefits (i.e., less hypotension, faster recovery) [53-57]. For a single-shot spinal anesthesia for cesarean delivery, most anesthesiologists use a dose of bupivacaine between 10 and 15 mg, in combination with opioids, sufentanil or fentanyl and morphine.

Conventional doses of hyperbaric bupivacaine are most often used to provide CSE anesthesia for cesarean delivery. However, a satisfactory block has been reported with plain bupivacaine drug doses as low as 4.5 mg [57]. Nonetheless, the CSE technique may use a lower dose of spinal bupivacaine (7.5 to 10 mg) followed by incremental injection of local anesthetic through the epidural catheter to achieve a T4 level of anesthesia [43,44], a procedure called sequential CSE. The purported advantage of this approach is a lower incidence of hypotension. With the sequential CSE technique, Thoren and colleagues observed a more gradual onset of hypotension and a lower initial anesthesia level with the spinal dose [44]. However, all parturients in the CSE group required additional doses of local anesthetic through the epidural catheter. The sequential CSE technique may be of particular advantage in certain high-risk parturients (e.g., significant cardiac disease) in whom avoidance of severe hypotension is pivotal.

Finally, the most common local anesthetic used for the initiation and maintenance of epidural anesthesia for cesarean delivery is 2% lidocaine with epinephrine. The epidural administration of lidocaine in concentrations less than 2%, or without the addition of epinephrine (which independently augments the analgesia through alpha-adrenergic receptor blockade), may result in anesthesia that is inadequate for surgery [58]. Surgical anesthesia can also be produced with epidural administration of 0.5% bupivacaine. Nevertheless, the slow onset of blockade and the risk of cardiovascular toxicity from unintentional intravascular injection or systemic absorption limit the contemporary use of this agent. The single-isomer, levorotatory local anesthetics, 0.5% to 0.75% ropivacaine and 0.5% levobupivacaine, may be preferable to racemic bupivacaine because of their better safety profiles. Except for the safety profile, there are no significant clinical advantages to these single-isomer local anesthetics when equipotent doses are administered. Similarly to spinal anesthesia, opioids (sufentanil or fentanyl and morphine) are also usually administered in combination with local anesthetics.

Although neuraxial techniques are typically preferred when anesthesia is provided for cesarean delivery, there are some clinical situations in which the administration of general anesthesia is considered the most appropriate option. The basic elements for preparation and care of the obstetric patient undergoing cesarean delivery also apply to the patient undergoing general anesthesia. The preanesthetic evaluation should focus on assessment of physical characteristics, particularly airway features, and comorbidities. Pregnancy-induced changes in the upper airway may be exacerbated during labor [59]. Importantly, failed intubation, failed ventilation and oxygenation, and pulmonary aspiration of gastric contents remain leading anesthesia-related causes of maternal death. Table 3 describes the main recommendations to general anesthesia for cesarean delivery.

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**Brief algorithm of preparation to general anesthesia for cesarean delivery**


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1. Perform preanesthetic assessment and obtain informed consent;
2. Prepare necessary medications and check equipment and monitors;
3. Perform a "time-out" to verify patient identity, position, operative site, and procedure;
4. Place patient supine with left uterine displacement;
5. Consider the use of a nonparticulate antacid orally within 20 minutes before induction or metoclopramide 10 mg and/or ranitidine 30 mg intravenously more than 30 minutes before induction;
6. Administer antibiotic prophylaxis (preferentially before skin incision);
7. Initiate monitoring (electrocardiogram, non-invasive arterial pressure monitoring and pulse oximetry);
8. Provide 100% oxygen with a tight-fitting face mask for 3 minutes or longer. Alternatively, instruct the patient to take 4 to 8 vital-capacity breaths immediately before induction of anesthesia;
9. After the abdomen has been prepared and operative drapes are in place, verify that the surgeon and assistant are ready to begin surgery;
10. Initiate rapid-sequence induction (thiopental 4 to 6 mg/kg or propofol 1.5 to 2.5 mg/kg and succinylcholine 1 mg/kg; wait up to 45 seconds; The use of cricoid pressure is still recommended;
11. Perform endotracheal intubation. Confirm correct placement of endotracheal tube by using capnography;
12. Provide maintenance of anesthesia (usually by using volatile anesthetics);
13. Treat hypotension episodes by using phenylephrine or ephedrine;
14. Observe and support delivery of baby;
15. Begin a small bolus (up to 3 units) followed by a continuous infusion of oxytocin; consider other uterotonic agents (e.g., methylergometrine, misoprostol, prostaglandin F2 $\alpha$ ) if uterine tone is inadequate. Monitor cautiously the amount of blood loss;
16. Adjust maintenance anesthesia technique after delivery of the infant (reduced concentration of a volatile anesthetic to avoid a significant reduction in the uterine tonus);
17. Consider the high risk of awareness and recall in these patients. Cogitate administration of benzodiazepines (e.g., midazolam);
18. Provide adequate multimodal analgesia and prophylaxis for postoperative nausea and vomiting;
19. Perform extubation when neuromuscular blockade is fully reversed and the patient is awake and responds to commands;
20. Evaluate postoperative signs and symptoms (e.g., pain, nausea, vomiting, shivering, etc).

OBS: This algorithm may need to be modified accordingly case-by-case circumstances (e.g., emergency care for cesarean delivery).

Table 3. Main recommendations to general anesthesia for cesarean delivery

### 3.3 Hemodynamic monitoring: main techniques and recent advances

During cesarean delivery with neuraxial anesthesia, ECG changes have a reported incidence of 25% to 60% and are believed to be due to hyperdynamic circulation, circulating catecholamines, or altered hormone concentration ratios [60,61]. However, the significance of the ECG findings as an indicator of cardiac pathology remains controversial, but measurement of cardiac troponin indicates that rarely obstetric patients experience myocardial ischemia [62]. In a prospective study of 254 healthy women undergoing cesarean delivery with spinal anesthesia, Shen and colleagues have shown that the incidence of first- and second-degree atrioventricular block was 3.5% for each, severe bradycardia was 6.7%, and multiple premature ventricular contractions was 1.2%. The investigators speculated that a relative increase in parasympathetic activity occurred as a result of spinal blockade of cardiac sympathetic activity. Most of the dysrhythmias were transient and resolved spontaneously [63]. However, prompt management with vasoactive drugs should be performed if dysrhythmias persist.

An indwelling urinary catheter is used in almost all women undergoing cesarean delivery [64]. A urinary catheter helps avoid overdistention of the bladder during and after surgery. In cases of hypovolemia and/or oliguria, a collection system that allows precise measurement of urine volume should be used.

In regard to central invasive hemodynamic monitoring, there is insufficient literature to examine whether pulmonary artery catheterization or minimally invasive methods to evaluate cardiac output (pulse-wave analysis methods) are associated with improved maternal, fetal, or neonatal outcomes in women with pregnancy-related hypertensive disorders [65]. Additionally, there is an important lack of evidence regarding the management of obstetric patients with central venous catheterization. However, the routine use of pulmonary artery catheterization, pulse-wave analysis methods to evaluate cardiac output or central venous does not reduce maternal complications in severely preeclamptic women [6]. Therefore, the decision to perform invasive hemodynamic monitoring should be individualized and based on clinical indications that include the patient's medical history and cardiovascular risk factors.

### 3.4 Intravenous fluid replacement and preloading

Numerous techniques have been attempted to prevent hypotension following spinal anesthesia, with varying success. The most important preventive measure is to ensure left uterine displacement so as to avoid the supine hypotensive syndrome [66]. Prehydration or preloading is not necessarily an effective measure to prevent hypotension and several strategies of prehydration have been used elsewhere [67-69]. Some studies have found a smaller incidence of hypotension in the prehydrated patients as compared with the control (no prehydrated) patients. However, the total amount of fluid and vasoconstrictors, and the severity of the hypotension usually not differ between groups [67-69]. Nevertheless, neonatal outcomes, as measured by Apgar score and umbilical cord blood gas and pH measurements, are improved when the parturient is prehydrated [70]. Although there are some conflicting findings, the literature still supports the use of intravenous fluid preloading for spinal anesthesia since it seems to reduce the frequency of maternal hypotension when compared with no fluid preloading. Of note, though fluid preloading

reduces the frequency of maternal hypotension, initiation of spinal anesthesia should not be delayed to administer a fixed volume of intravenous fluid.

Colloid prehydration may be promising, but still deserves further study. Ueyama and colleagues demonstrated that the incidence of hypotension was 75% in those who received lactated Ringer's, 58% in those who received 500 mL of hydroxyethylstarch, and only 17% in those who received 1000 mL of hydroxyethylstarch [69]. Future studies should address the use of colloids in the obstetric setting in order to demonstrate efficacy and safety.

### **3.5 Rationale for the use of vasoconstrictors**

In regard to the use of vasoconstrictors in the obstetric setting especially for spinal anesthesia, the literature supports the administration of ephedrine, but suggests that phenylephrine is effective in reducing maternal hypotension during neuraxial anesthesia for cesarean delivery. The literature is equivocal regarding the relative frequency of patients with breakthrough hypotension when infusions of ephedrine are compared with phenylephrine; however, lower umbilical cord pH values are reported after ephedrine administration as compared to the  $\alpha_1$ -agonist phenylephrine. Although recent data indicates that  $\alpha_1$ -agonists are more effective to avoid hypotension following spinal anesthesia for cesarean delivery, ephedrine is acceptable for treating hypotension during neuraxial anesthesia. Therefore, intravenous ephedrine and phenylephrine are both acceptable drugs for treating hypotension during neuraxial (spinal or epidural) anesthesia. In the absence of maternal bradycardia, phenylephrine may be preferable because of improved fetal acid-base status in uncomplicated pregnancies. Of note, some countries routinely use metaraminol as an  $\alpha_1$ -agonist instead of phenylephrine in the obstetric setting without significant adverse events. This drug seems to be similarly effective as phenylephrine. Of note, prophylactic intravenous ephedrine or phenylephrine before spinal anesthetic placement has been studied to prevent hypotension, and is generally not recommended because of the risk of reactive hypertension [71,72].

## **4. Recovery from anesthesia**

### **4.1 Postoperative (post-cesarean) analgesia: the role of neuraxial opioids**

For improved postoperative analgesia after cesarean delivery during epidural anesthesia, the literature supports the use of epidural opioids compared with intermittent injections of intravenous or intramuscular opioids. However, a higher frequency of pruritus was found with epidural opioids. The literature is insufficient to evaluate the impact of epidural opioids compared with intravenous PCA. In addition, the literature is insufficient to evaluate spinal opioids compared with parenteral opioids. However, there is sufficient evidence that neuraxial opioids improve postoperative analgesia and maternal satisfaction. Therefore, we can argue that, for postoperative analgesia after neuraxial anesthesia for cesarean delivery, neuraxial opioids are preferred over intermittent injections of parenteral opioids [6]. Studies are equivocal regarding doses regimen, especially for epidural opioids (morphine). In spinal anesthesia for cesarean delivery, morphine doses are usually between 60 and 100  $\mu$ g. Epidural morphine is usually administered in doses between 2 and 3 mg. However, controversy exists and new studies regarding efficacy and adverse effects are warranted.

#### **4.2 Oral intake, removal of urinary catheter and discharge**

Mangesi and Hofmeyr performed a systematic review of six randomized clinical trials comparing early with delayed oral intake of fluids and foods after cesarean delivery [73]. The authors found that the early consumption (within 4 to 8 hours) was associated with a shorter time to return of bowel sounds and a shorter hospital stay. No differences were reported in nausea and vomiting, abdominal distention, time to bowel activity, paralytic ileus, or need for analgesia.

There are no differences in the incidence of urinary retention after general anesthesia and epidural anesthesia following cesarean delivery [74]. Risk factors for postpartum urinary retention after cesarean delivery include the use of postoperative opioid analgesia (particularly when given via an epidural catheter), multiple gestations, and a low body mass index [75]. Most urinary catheters are removed either immediately following cesarean delivery, before discharge from the postoperative care unit or within 24 hours, but there are no differences between these options in regard to postoperative urinary retention, infection, dysuria, urgency, fever, or length of hospital stay [76].

In regard to the postoperative discharge, the anesthesiologist should routinely assess for recovery of motor and sensory function if a neuraxial technique was administered. Patients should be reassured that breast-feeding is safe, even after general anesthesia, and that postoperative analgesics have a favorable safety profile. Early mobility and ambulation should be stimulated.

#### **5. Cesarean delivery: Anesthetic complications**

The main anesthetic complications in cesarean delivery include, but are not limited to: hypotension, failure of neuraxial blockade, high blockade levels, dyspnea, nausea and vomiting, postoperative pain, pruritus, and shivering.

Hypotension is a common consequence of neuraxial anesthetic techniques and, when severe and sustained, can lead to impairment of uteroplacental perfusion, resulting in fetal hypoxia, acidosis, and neonatal depression [77]. Severe maternal hypotension can also have adverse maternal outcomes, including unconsciousness, pulmonary aspiration, apnea, bradycardia, and even cardiac arrest. The definition of maternal hypotension is controversial, but many investigators accept the following definition: a decrease in systolic blood pressure of more than 20% from baseline measurements or a systolic blood pressure lower than 100 mmHg [78]. Neuraxial anesthetic techniques produce hypotension through blockade of sympathetic nerve fibers, which control vascular smooth muscle tone. Preganglionic sympathetic fiber blockade primarily causes an increase in venous capacitance, which shifts a major portion of blood volume into the splanchnic bed and the lower extremities, thereby reducing venous return to the heart. The rate and extent of the sympathetic involvement, and subsequently the severity of hypotension, are determined by the onset and spread of the neuraxial blockade [79]. Consequently, hypotension may be less common with epidural anesthesia than with spinal anesthesia because of the slower onset of blockade. The delayed onset of hypotension with epidural anesthesia may also allow earlier treatment before hypotension becomes more severe.

A failure of neuraxial blockade can be defined as blockade insufficient in extent, density, or duration to provide anesthesia for cesarean delivery. Approximately 4% to 13% of epidural and 0.5% to 4% of spinal anesthetics fail to provide sufficient anesthesia for the initiation or completion of cesarean delivery [33,80]. Epidural techniques are more often associated with failure, given the fact that the catheter is often placed during early labor, and over time the catheter may migrate out of the epidural space. Factors that may correlate with failed extension of labor epidural anesthesia for cesarean delivery include a higher number of bolus doses for the provision of labor analgesia, patient characteristics (e.g., obesity, catheter positioning), and the time elapsed between placement of the catheter and cesarean delivery [33,80].

It is not uncommon for the parturient to report mild dyspnea or reduced ability to cough, especially if the neuraxial blockade has achieved higher than a T<sub>4</sub> level. If impaired phonation, unconsciousness, respiratory depression, or significant impairment of ventilation occurs, administration of general anesthesia is recommended. High neuraxial blockade may also result in cardiovascular collapse, including severe bradycardia and hypotension. This complication may be caused by several mechanisms, including an exaggerated spread of spinal or epidural drugs and unintentional intrathecal or subdural administration of an “epidural dose” of local anesthetic.

Nausea and vomiting are regulated by the chemoreceptor trigger zone and the vomiting center, which are located in the area postrema and the medullary lateral reticular formation, respectively. The vomiting center receives impulses from the vagal sensory fibers in the gastrointestinal tract, the semicircular canals and ampullae (labyrinth) of the inner ear, higher cortical centers, the chemoreceptor trigger zone, and intracranial pressure receptors. Impulses from these structures are influenced by dopaminergic, muscarinic, tryptaminergic, histaminic, and opioid receptors, which are subsequently the targets for antiemetic agents. Efferent impulses from the vomiting center are transmitted through the vagus, phrenic, and spinal nerves to the abdominal muscles, which causes the physical act of vomiting [81].

Preventing maternal hypotension may be the best means of preventing nausea and vomiting. Additionally, several options exist for the pharmacologic prophylaxis of nausea and vomiting, and several different classes of drugs are available. Although various algorithms have been developed to prevent postoperative nausea and vomiting, primarily targeting the nonpregnant patient population, none has been universally successful [82]. However, the prophylactic use of these agents either before or after cord clamping during cesarean delivery with neuraxial anesthesia has been demonstrated to be highly effective. Notably, multimodal therapies combining different medications may eventually prove the most effective. Several drugs have been shown to be effective, but most frequently used include intravenous ondansetron 4 mg after cord clamping, metoclopramide 10 mg prior to surgery or after cord clamping, droperidol 0.625 - 1.25 mg at end of surgery, dimenhydrinate 25 - 50 mg, and/or dexamethasone 4 - 8 mg, both possibly after cord clamping or at end of surgery.

Postoperative pain may have at least two components, somatic and visceral. A multimodal approach seems to provide the most effective post-cesarean delivery analgesia. Such an approach often includes administration of a nonsteroidal anti-inflammatory drug (NSAID), acetaminophen and dipyrone. Concerns have been expressed regarding possible adverse

effects (platelet dysfunction, uterine atony), but these agents are widely used and seem to be safe. Some investigators have expressed concern about the role of NSAIDs on breast-feeding, but the American Academy of Pediatrics has stated that ibuprofen and ketorolac are compatible with breast-feeding [83].

The administration of opioids can cause pruritus. The incidence is as high as 30% to 100%, and pruritus is more commonly observed when opioids are administered spinally than epidurally. Pruritus is typically self-limited and may be generalized or localized to regions of the nose, face, and chest. Opioid-induced pruritus appears to be influenced by the particular combination of local anesthetic and opioid; of interest, the addition of epinephrine to an opioid–local anesthetic solution appears to augment the pruritus [84]. Notably, this side effect does not represent an allergic reaction to the neuraxial opioid. If flushing, urticaria, rhinitis, bronchoconstriction, or cardiac symptoms also occur, allergic reaction to another drug should be considered as a differential diagnosis. The cause of neuraxial opioid-induced pruritus is not known, although multiple theories have been proposed. They include  $\mu$ -opioid receptor stimulation at the medullary dorsal horn, antagonism of inhibitory transmitters, and activation of an “itch center” in the central nervous system [85]. Pharmacologic prophylaxis or treatment of pruritus may include an opioid antagonist, an opioid agonist/antagonist, droperidol, a serotonin antagonist (e.g., ondansetron), and/or a subhypnotic dose of propofol [85]. Yeh and colleagues observed that ondansetron significantly reduced the incidence of spinal morphine-induced pruritus [86]. Although opioid antagonists, such as naltrexone and naloxone, and partial agonist/antagonists, such as nalbuphine, are probably the most effective treatments for pruritus, the use of any of these agents, either as a single dose or in continuous intravenous infusion, may also reverse analgesia. Antihistamines are often prescribed but are largely ineffective because the mechanism of pruritus is not related to histamine release.

Intraoperative and postoperative shivering may also have several etiologies but is usually related to a decrease in central temperature related to peripheral vasodilation. Several treatments are effective, but most frequently used include intravenous meperidine 10 - 30 mg, clonidine 15 - 150  $\mu$ g, and alfentanil up to 250  $\mu$ g [87].

## **6. Anticoagulation, coagulopathies and regional anesthesia in obstetrics**

Concern exists that an epidural/spinal hematoma may develop after the administration of neuraxial anesthesia in patients with coagulopathy or using anticoagulants. There are only a few published cases of epidural hematoma after the administration of neuraxial anesthesia in pregnant patients [88,89]. This fact suggests that epidural hematoma after neuraxial anesthesia either is very uncommon or is underreported. However, in view of the serious effects of an epidural hematoma, the risks and benefits of performing neuraxial anesthesia should be carefully considered in a patient with either clinical or laboratory evidence of coagulopathy or pregnant women using anticoagulants.

Clearly, severe coagulopathy represents a well-known contraindication to the administration of neuraxial anesthesia, even in obstetric patients. The anesthesiologist can use laboratory tests (e.g., prothrombin time/International Normalized Ratio, partial thromboplastin time, activated clotting time measurements or thromboelastography) to assess the extent of anticoagulation and the effectiveness of reversal in patients receiving



standard unfractionated heparin or oral anticoagulation therapy. If use of a neuraxial anesthetic technique is considered in a patient with a congenital coagulopathy, results of the factor assays should be within the normal range before neuraxial anesthesia administration [90].

Thrombocytopenia is relatively common in pregnant women with severe preeclampsia. Asymptomatic thrombocytopenia also may occur in healthy obstetric patients. Previous studies have reported that administration of neuraxial anesthesia is safe in healthy pregnant women with thrombocytopenia (i.e., platelet count less than 100,000/mm<sup>3</sup>). In this context, the anesthesiologist should always consider the following factors: clinical evidence of bleeding, recent platelet count, recent changes in the platelet count, quality of platelets, coagulation factors, and, most importantly, the risk/benefit ratio of performing neuraxial anesthesia [91].

Most pregnant women who require long-term anticoagulation receive low molecular weight heparin (LMWH) or standard unfractionated heparin throughout pregnancy. LMWH (e.g., enoxaparin) is considered to be more efficacious for thromboprophylaxis than standard unfractionated heparin and has been used safely in pregnant women [92]. However, several cases of epidural/spinal hematoma after neuraxial anesthesia in non-obstetric patients receiving LMWH have been reported [93,94]. This apparent increase in the risk for an epidural hematoma may be related to the use of higher doses of LMWH and its relatively greater bioavailability and longer half-life in comparison with standard unfractionated heparin. Guidelines recommend that in patients receiving LMWH for thromboprophylaxis, needle placement should occur at least 10 to 12 hours after the last LMWH dose. In patients receiving higher doses of LMWH (e.g., enoxaparin 1 mg/kg every 12 hours or enoxaparin 1.5 mg/kg daily), needle placement should not occur until at least 24 hours after the last dose of LMWH [92]. In patients receiving a single daily dose of LMWH thromboprophylaxis, the first postoperative LMWH dose should be administered only 6 to 8 hours after surgery. An indwelling epidural catheter may be safely maintained in these patients; however, it should be removed at least 12 hours after the last dose of LMWH, and the next dose of LMWH should be administered at least 2 hours after catheter removal. In patients receiving higher doses of LMWH, the first dose of LMWH should be delayed for 24 hours postoperatively, and an indwelling catheter should be removed at least 2 hours before initiation of LMWH therapy [92].

There is a large experience with the use of standard unfractionated heparin and a large number of patients have received neuraxial anesthesia while receiving subcutaneous thromboprophylaxis with standard unfractionated heparin, without significant neurologic complications. In this context, guidelines recommend that subcutaneous thromboprophylaxis with standard unfractionated heparin does not contraindicate the use of neuraxial anesthesia. However, the platelet count should be assessed before the administration of neuraxial anesthesia or catheter removal in patients who have received standard unfractionated heparin for more than 4 days [92].

If oral anticoagulants (e.g., warfarin) are administered during pregnancy, it is usually replaced by LMWH or standard unfractionated heparin before the onset of labor. If a pregnant woman begins labor while she is still taking oral anticoagulants, the effects can be reversed by intramuscular administration of vitamin K. Because reversal of anticoagulation

requires time for the synthesis of new procoagulants, acute reversal can be accomplished by the administration of 10 to 20 mL/kg of fresh frozen plasma [91].

Low-dose aspirin does not significantly prolong the bleeding time in pregnant women [95]. Therefore, there is no recommendation to obtain a bleeding time measurement in patients who have received low-dose aspirin during pregnancy. Moreover, a large number of women receiving low-dose aspirin therapy for the prevention or treatment of preeclampsia have undergone epidural analgesia for labor and delivery without complications [96].

Notably, the contraindication of regional anesthesia in pregnant women displaying mild or isolated abnormalities in blood coagulation tests is somewhat controversial. However, it is clear that the prophylactic administration of low-molecular-weight heparin is a clinical risk factor that warrants caution in the administration of neuraxial anesthesia. The anesthesiologist should weigh the risks and benefits of neuraxial anesthesia and general anesthesia for the individual patient. It is preferable not to administer neuraxial anesthesia to a patient with a persistent laboratory coagulation abnormality. However, in selected circumstances, neuraxial anesthesia may be offered to a patient with an isolated laboratory abnormality and no clinical evidence of coagulopathy. In such patients, frequent neurologic examinations should be performed to facilitate the early detection of an epidural hematoma during the postpartum period.

## **7. Contraindications to regional (neuraxial) anesthesia in obstetrics**

Regional (neuraxial) anesthesia is usually considered the first choice for most cesarean delivery procedures. However, similarly to other non-obstetric procedures, some contraindications can be pointed out. Contraindications for neuraxial anesthesia in the obstetrics setting usually include the following: patient refusal or inability to cooperate, severe coagulopathy, uncorrected maternal hypovolemia or significant hemodynamic instability, increased intracranial pressure, skin or soft tissue infection at the site of needle puncture. Severe anatomical abnormalities of the spine could also be related to significant difficulties to provide neuraxial anesthesia. The often-cited relative contraindication of preexisting neurologic disease is not usually based on medical criteria but rather on legal considerations [97]. The anesthesiologist should always weigh the risks and benefits of neuraxial anesthesia for each patient.

## **8. Summary of the main recommendations in anesthesia for cesarean delivery: the anesthetic procedure can change obstetric outcomes?**

### **8.1 Perianesthetic evaluation**

- Before providing anesthesia care, conduct history a focused on relevant obstetric history, maternal health and anesthetic history;
- Brief physical examination focused on airway and heart and lung examination and back examination when neuraxial anesthesia is planned;
- Baseline blood pressure measurement (at least two measures);
- Order a platelet count, blood type, and cross-match based on a patient's history, physical examination, clinical signs, and anticipated hemorrhagic complications. Of note, a routine platelet count and blood cross-match are not necessary in the healthy parturient and uncomplicated parturients;

- Oral intake of modest amounts of clear liquids may be allowed for uncomplicated patient undergoing elective cesarean delivery up to 2 h before induction of anesthesia. Pregnant women with additional risk factors for aspiration may have further restrictions of oral intake, determined on a case-by-case basis. Women undergoing elective cesarean delivery should undergo a fasting period for solids of 6–8 h depending on the type of food ingested;
- In selected patients, consider preanesthetic administration of nonparticulate antacids (sodium citrate), H<sub>2</sub> receptor antagonists (ranitidine), and/or metoclopramide for aspiration prophylaxis;

### 8.2 Anesthesia for cesarean delivery

- Equipment and support personnel available in the delivery operating room should be comparable to those available in the main operating rooms;
- Equipment and support for the treatment of potential complications (e.g., failed intubation, hypotension, etc) should be available in the delivery operating room;
- Appropriate equipment and support personnel should be available to postoperative care for obstetric patients recovering from major neuraxial or general anesthesia;
- Neuraxial techniques are preferred to general anesthesia for most cesarean deliveries. The decision to use a particular anesthetic technique should be individualized based on anesthetic, obstetric, or fetal risk factors, the preferences of the patient, and the judgment of the anesthesiologist;
- If spinal anesthesia is chosen, pencil-point spinal needles should be used instead of cutting-bevel spinal needles;
- An indwelling epidural catheter may provide equivalent onset of anesthesia compared with initiation of spinal anesthesia for urgent cesarean delivery
- General anesthesia may be the most appropriate choice in some circumstances (e.g., profound fetal bradycardia, ruptured uterus, severe hemorrhage, severe placental abruption);
- Intravenous fluid preloading may be used to reduce the frequency of maternal hypotension following spinal anesthesia for cesarean delivery. However, initiation of spinal anesthesia should not be delayed to administer a fixed volume of intravenous fluid;
- Uterine displacement (usually left displacement) should be maintained until delivery regardless of the anesthetic technique used;
- Intravenous ephedrine and alpha<sub>1</sub>-agonists (phenylephrine or metaraminol) are both acceptable drugs for treating hypotension during neuraxial anesthesia. In the absence of maternal bradycardia, alpha<sub>1</sub>-agonists, particularly phenylephrine, may be preferable because of improved fetal acid-base status in uncomplicated pregnancies;

### 8.3 Recovery from cesarean delivery

- For postoperative analgesia after neuraxial anesthesia for cesarean delivery, neuraxial opioids are preferred over intermittent injections of parenteral opioids

## 9. References

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This book provides broad, science-based information regarding the most common major surgical procedure performed, i.e. Cesarean Delivery. The book provides relevant scientific literature regarding epidemiology and rates of cesarean delivery in low and high income countries and the impact of the disparities in the rate of cesarean delivery between countries. In addition, the book systematically reviews the relevant scientific literature regarding all perioperative considerations with a broad cover of anesthetic techniques, drugs and difficulties that anesthesiologists may encounter during cesarean delivery. Care of the neonate after cesarean and crucial guidelines for obese women undergoing cesarean are also provided. The book was written by distinguished experts from different disciplines to ensure complete and accurate coverage of the recent scientific and clinical advances and to bring care providers and purchasers up to date including essential information to help improve health care quality.

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