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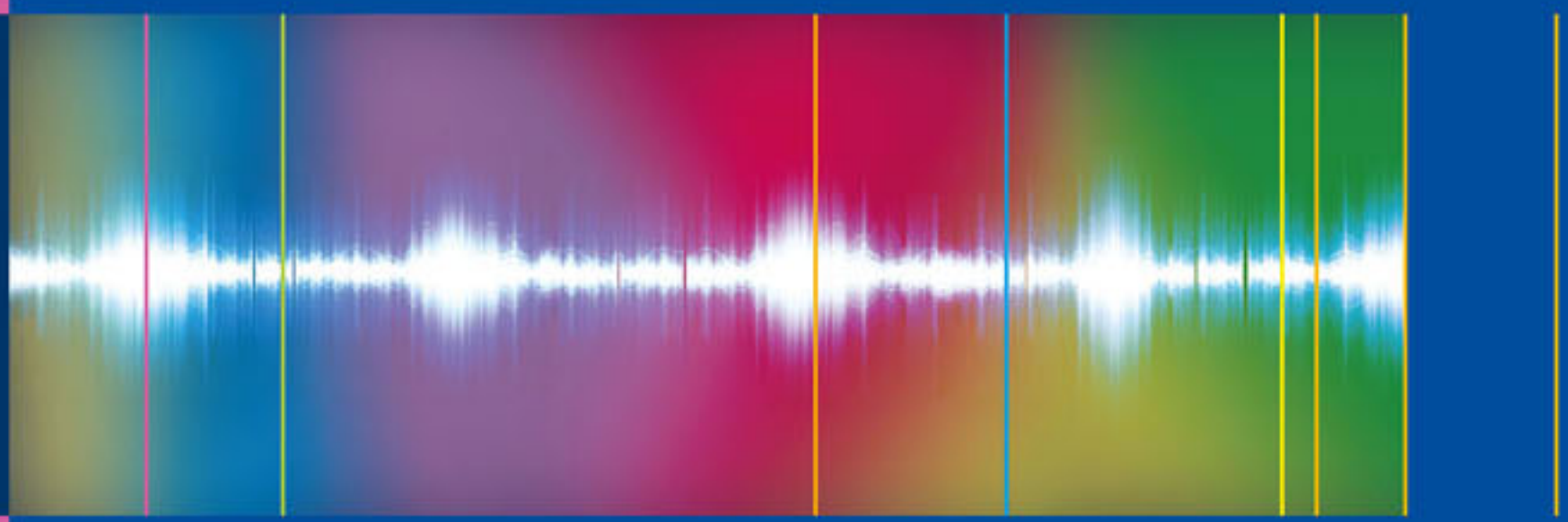

Obstetric Anesthesia Handbook

Fifth Edition

Springer

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Preface to the Fifth Edition

It is a great honor for us to join Dr. Sanjay Datta in presenting the fifth edition of *The Obstetric Anesthesia Handbook*. As former students and now colleagues of our mentor, we have attempted to update this classic and widely read book to reflect the constantly evolving face of obstetric anesthesiology. It is astounding to envision the initial writing of this text, nearly 20 years ago, in an era before the ubiquitous availability of online search tools, downloadable papers, and searchable textbooks. The early editions were formed predominantly out of Dr. Datta's personal command of the field, its literature, and his personal teaching files. Many benefited from the depth and breadth of his wisdom presented in the original *Handbook*, and it is now our privilege to help pass on this work to the next generation of residents, fellows, and obstetric anesthesia practitioners around the world. We have attempted to retain the compact style of the original single-author version, while adding some newer material, reorganizing some chapters to enhance their utility, updating references, and revising some figures and appendices. We hope you will find it as helpful in your practice as it is in ours.

Scott Segal, MD
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Preface to the First Edition

One of the major "perks" of an academic anesthesiologist is the opportunity to interact with residents and fellows. Most of them are bright, energetic, and hardworking individuals. During my professional life, I enjoyed my dealings with this special group, and their enthusiasm in obstetric anesthesia is the basis for the germination of this project.

Parturients are different from their nonpregnant counterparts in various ways. Their expectations, demands, and needs make obstetric anesthesia more challenging and also gratifying. This book basically deals with these aspects at a level that I found stimulating to the residents as well as fellows.

There are 19 chapters in this book that address the various aspects of maternal physiology, perinatal pharmacology, and, ultimately, anesthetic techniques for different procedures; my hope is that this is done in a concise manner. Every effort has been made to discuss the controversial issues of anesthetic techniques covering the majority of problems that might arise.

It is my deepest desire that this book be both helpful and stimulating to residents, fellows, and my contemporaries. To this end, periodic updates of this manual will be made to keep its contents current and to address topics of interest and controversy.

I want to express my gratitude to a few individuals without whom this project would remain incomplete. My thanks are directed to Dr. Knapp for his very eloquently expressed views regarding medicolegal aspects of obstetric anesthesia. My special thanks go to Ms. Vehring, whose editorial assistance was extremely necessary. Finally, I must also express my gratitude to Ms. Racke for her graphic illustrations and Ms. Russo and Ms. Spelling for secretarial help.

Sanjay Datta, MD, F.F.A.R.C.S. (Eng)

Contents

1
Maternal Physiological Changes During Pregnancy, Labor, and the Postpartum Period

Parturients undergo remarkable changes during pregnancy, labor, and the immediate postpartum period that can directly affect anesthetic techniques; hence a broad knowledge of these changes is essential for optimum management of these women.

Changes in the Hematological System

Maternal blood volume increases during pregnancy, and this involves an increase in plasma volume as well as in red cell and white cell volumes.[1] *The plasma volume increases by 40–50%, whereas the red cell volume increases by only 15–20%, which causes a "physiological anemia of pregnancy"* (normal hemoglobin 12 g/dL; hematocrit 35).[2] Because of this hemodilution, blood viscosity decreases by approximately 20%. The exact mechanism of this increase in plasma volume is unknown. However, several mediators such as

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renin–angiotensin–aldosterone, atrial natriuretic peptide, estrogen, progesterone, and nitric oxide may be involved. The most likely hypothesis attributes the increase to an "underfill" state caused by initial vasodilation, which stimulates hormones such as renin, angiotensin, and aldosterone to cause fluid retention.[3] Alternatively, some have proposed an "overfill" state characterized by an early increase in sodium retention (due to an increase in mineralcorticoids) that leads to fluid retention, causing an increase in blood volume, followed subsequently by vasodilation.

Blood volume increases further during labor, as uterine contractions squeeze blood out of the intervillious space and into the central circulation. After delivery, involution of the uterus and termination of placental circulation causes an autotransfusion of approximately 500 mL of blood.

Levels of clotting factors I, VII, VIII, IX, X, and XII and fibrinogen are elevated during pregnancy as well. Platelet production is increased, thrombopoietin levels are increased,[4] and platelet aggregation measured in vitro is likewise increased; indices of platelet destruction are also increased. The overall effect of these changes is variable, but prospective observations have reported a statistically significant fall in platelet count as pregnancy progresses, with 7.6% of women having a count less than 150,000 and 1% less than 100,000 at term.[5] Endogenous anticoagulants, such as protein S, are decreased in normal pregnancy and there is acquired resistance to activated protein C during pregnancy, adding to the prothrombotic state. Fibrinolysis is impaired in normal pregnancy due to placentally derived plasminogen activator inhibitor (PAI), but returns to normal following delivery of the placenta. Overall indices of coagulation indicate that normal pregnancy is a hypercoagulable state.[6]

Clinical Implications

Increased blood volume and enhanced coagulation serve several important functions: (1) the increased circulatory needs of the enlarging uterus and growing fetus and placenta are met and (2) the parturient is protected from bleeding at the

time of delivery. Anesthesiologists should consider the enlarged blood volume when making decisions on fluid and blood replacement in the peripartum period. Parturients become hypercoagulable as gestation progresses and are at increased risk of thromboembolism. After a rapid mobilization and diuresis of some fluid in the first few postpartum days, blood volume slowly returns to normal over 8 weeks.

Changes in the Cardiovascular System

An increase in cardiac output is one of the most important changes of pregnancy. *Cardiac output increases by 30–40% during pregnancy, and the maximum increase is attained around 24 weeks' gestation.*[7] The increase in heart rate occurs first (by the end of the first month of pregnancy) and plateaus at an increase of 10–15 beats per minute by 28–32 weeks' gestation. Stroke volume increases by mid-first trimester and progressively increases through the second trimester. Echocardiography demonstrates increases in end-diastolic chamber size and total left ventricular wall thickness but no change in end-systolic volume, so ejection fraction is increased. Cardiac output can vary depending on the uterine size and maternal position at the time of measurement. The enlarged gravid uterus can cause aortocaval compression and reduced cardiac filling while the pregnant woman is in the supine position (Fig. 1-1), leading to an underestimation of cardiac function. Normal pregnant women exhibit a marked increase in femoral venous and inferior vena caval pressures. Collateral vessels maintain atrial filling but lead to engorgement of veins, including the epidural venous (Batson's) plexus.

Filling pressures (CVP, pulmonary capillary wedge pressure, LV end-diastolic pressure) do not change despite the increased cardiac dimensions, due to myocardial remodeling during gestation. Systemic vascular resistance is decreased approximately 20%. Blood pressure never increases in normal pregnancy, and systolic and diastolic blood pressures decrease by approximately 8 and 20%, respectively, on average.[9] Pregnancy hormones (estradiol and progesterone), prostacyclin, and nitric

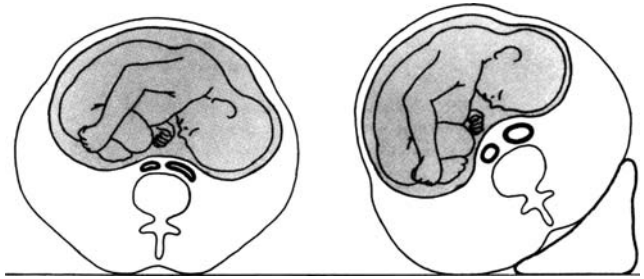

Figure 1–1. Aortocaval compression. (From Chestnut.[8] Used with permission from Elsevier.)

oxide all may play a role in the reduction in blood pressure observed despite an increase in cardiac output.

Cardiac output increases further during labor, up to 50% higher than pre-labor values, although effective analgesia can attenuate some of this increase. In the immediate postpartum period, cardiac output increases maximally and can rise 80% above pre-labor values and approximately 150% above nonpregnant measurements. An increase in stroke volume as well as in heart rate maintains the increased cardiac output.

The heart is displaced to the left and upward during pregnancy because of the progressive elevation of the diaphragm by the gravid uterus. The electrocardiogram of normal parturients may include (1) sinus tachycardia or benign dysrhythmias, (2) depressed ST segments and flattened T waves, (3) left axis deviation, and (4) left ventricular hypertrophy. Auscultation frequently reveals a systolic murmur of tricuspid or mitral regurgitation, and a third or fourth heart sound.

Cardiac output, heart rate, and stroke volume decrease to pre-labor values 24–72 h postpartum and return to nonpregnant levels within 6–8 weeks after delivery.[10]

Clinical Implications

An increased cardiac output might not be well tolerated by pregnant women with valvular heart disease (e.g., aortic or mitral stenosis) or coronary arterial disease. *Decompensation in*

myocardial function can develop at 24 weeks' gestation, during labor, and especially immediately after delivery.

Engorgement of the epidural venous plexus increases the risk of intravascular catheter placement in pregnant women; direct connection of the azygos system to the heart as well as brain also increases the risks of local anesthetic cardiovascular and central nervous system toxicity.

Changes in the Respiratory System

Changes in respiratory parameters start as early as the fourth week of gestation. Minute ventilation is increased at term by about 50% above nonpregnant values. The increase in minute ventilation is mainly due to an increase in tidal volume (40%) and, to a lesser extent, an increase in the respiratory rate (15%).[11] Alveolar ventilation is greatly increased as the tidal volume increases without any change in the ratio of dead space to tidal volume (V_D/V_T). At term PCO_2 is decreased to 32–35 mmHg, although renal excretion of bicarbonate keeps arterial pH normal. Increased progesterone concentrations during pregnancy likely stimulate increased respiration, even before an increase in metabolic rate.[12] Oxygen consumption and carbon dioxide production increase by approximately 60% over prepregnant values. PaO_2 is increased in early pregnancy due to a decrease in PCO_2.

Functional residual capacity, expiratory reserve volume, and residual volume are decreased at term (Fig. 1-2). These changes are related to the cephalad displacement of the diaphragm by the large gravid uterus. Inspiratory capacity increases somewhat because of increase in tidal volume and inspiratory reserve volume. Vital capacity is unchanged. Total lung capacity is only slightly reduced because chest circumference increases. Closing capacity (CC) does not change, but the reduction in FRC contributes to a tendency toward earlier desaturation, as lung volume more easily falls below CC.

Anatomic changes also accompany pregnancy. The respiratory mucous membranes become vascular, edematous, and friable. The voice may deepen and there is a progressive increase in the Mallampati score during gestation and labor.[13]

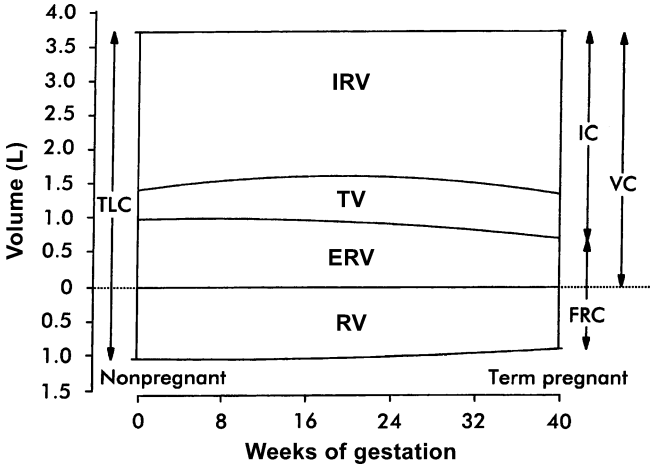

Figure 1–2. Pulmonary volume and capacity changes in pregnancy. (From Chestnut.[8] Used with permission from Elsevier.)

In labor, minute volume further increases in the absence of pain relief, and PCO_2 may decrease to 17 mmHg. Opioids somewhat attenuate this change, but epidural analgesia does so more completely. In the second stage, maternal expulsive efforts increase ventilation, even in the presence of effective regional analgesia.[14,15]

FRC changes return to normal 1–2 weeks postpartum, accompanying the reduction in uterine size. All other respiratory parameters return to nonpregnant values within 6–12 weeks postpartum.

Clinical Implications

Decreased FRC as well as increased oxygen consumption can cause a rapid development of maternal hypoxemia during apnea. Decreased FRC decreases the time for denitrogenation and speeds the uptake of inhaled anesthetics.

Because of the increased edema, vascularity, and friability of the mucous membrane, one should try to avoid nasal

intubation in pregnant women, and smaller endotracheal tubes should be used for oral intubation.

Maternal alkalosis associated with decreased $PaCO_2$ values due to hyperventilation as a result of labor pain can cause fetal acidosis because of (1) decreased uteroplacental perfusion due to uterine vasoconstriction and (2) shifting of the maternal oxygen dissociation curve to the left.

Changes in the Gastrointestinal System

The enlarging uterus displaces and disrupts the lower esophageal sphincter, and progesterone relaxes this high-pressure zone, causing a progressive increase in the incidence of heartburn (up to 80% at term). An increase in gastric pressure due to mechanical compression also contributes to heartburn. Despite the prevalence of this symptom, total acid production is decreased (although placental production of gastrin increases the total concentration of this hormone).

Gastric emptying is normal throughout pregnancy, as measured by acetaminophen absorption, ultrasound, dye-dilution, and radiographic techniques. Intestinal transit time is increased, leading to frequent complaints of constipation in pregnant women. Studies of gastric pH and volume in pregnant and nonpregnant women show no differences in the proportion of women meeting "at risk" criteria (pH <2.5, volume >25 ml[16]) for pulmonary aspiration of gastric contents.[8]

Labor fundamentally alters this pattern. Gastric emptying time is significantly slower during labor and hence gastric volume is increased. Opioids administered by any route will further increase the gastric emptying time. Studies demonstrate solid food in the stomachs of laboring women even after 18 h of fasting.[17] Gastric emptying remains abnormal on the first postpartum day but returns to normal on the second day.

Hepatic transaminases, bilirubin, and LDH are increased slightly in pregnancy. Alkaline phosphatase is markedly increased (2–4 fold), but due to placental production, not hepatic changes. *Serum cholinesterase activity is reduced 24% before delivery and reaches a nadir (33% reduction) on the third postpartum day*[14] (Fig. 1-3). Approximately 11% of post-

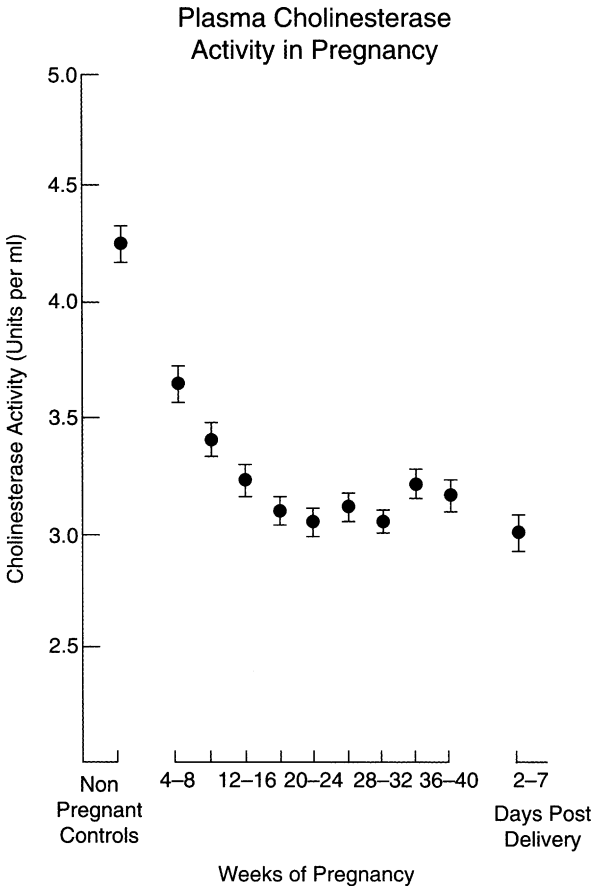

Figure 1–3. Plasma cholinesterase activity in pregnancy. (From Cohen.[18] Used with permission from Elsevier.)

partum women exhibit clinically deficient activity, manifest as an exaggerated response to normal doses of succinylcholine. *Even with this lower activity, normal dosing of succinylcholine for intubation is recommended when general anesthesia is required, though use of a peripheral nerve stimulator seems prudent.*

Gallbladder function and emptying are impaired during pregnancy, and there is evidence that pregnant women may be more prone to gallstones.

Clinical Implications

Pregnant women *in labor* should always be considered to have a full stomach irrespective of the time of their last meal. General anesthesia should be avoided when possible, and routine precautions (rapid sequence induction and endotracheal intubation) should be employed when general anesthesia is unavoidable. The routine use of nonparticulate antacid is important before cesarean section and before induction of regional anesthesia, and one should allow for proper mixing of the antacid and stomach contents. Pregnant women who are not in labor and who do not have other risk factors for aspiration may not require such treatment.

Changes in the Renal System

The glomerular filtration rate is increased during pregnancy because of increased renal plasma flow.[19] A rise in the filtration rate decreases plasma blood urea nitrogen (BUN) and creatinine concentrations by about 40–50%, to approximately 8–9 mg/dL and 0.5–0.6 mg/dL, respectively. Tubular reabsorption of sodium is increased. However, glucose and amino acids might not be absorbed as efficiently; hence glycosuria (up to 300 mg/day) and aminoaciduria may develop in normal gestation. The renal pelvis and ureters are dilated, and peristalsis is decreased. Physiological diuresis during the postpartum period occurs between the second and fifth days. The glomerular filtration rate and BUN concentration slowly return to nonpregnant values by the sixth postpartum week.

Clinical Implications

Normal nonpregnant values of BUN and Cr in parturients suggest abnormal kidney function.

Changes in the Central and Peripheral Nervous Systems

The central and peripheral nervous systems undergo significant changes during pregnancy. MAC is decreased by 25–40% during pregnancy.[20] Increased progesterone and endorphin concentrations during pregnancy have been implicated as a cause of this change. However, a few studies have shown that endorphin concentrations do not increase until the onset of active labor,[21] so this cannot explain early decreases in MAC. By injecting exogenous progesterone in oophorectomized rabbits, a decrease in MAC was observed when compared with control animals.[22]

A wider dermatomal spread of sensory anesthesia was observed in parturients following the use of epidural anesthesia as compared with nonpregnant age-matched controls.[23] The difference was explained by a reduction in epidural space volume caused by an engorged epidural venous plexus due to aortocaval compression. However, a subsequent report showed that this difference exists even during early pregnancy (8–12 weeks) when one might not expect any mechanical obstruction by the small gravid uterus,[24] and epidural venous engorgement later in pregnancy appears to reduce CSF volume, not epidural extravascular volume. The factors suggested were (1) compensated respiratory alkalosis of pregnancy, (2) reduced plasma and cerebrospinal fluid (CSF) protein levels during pregnancy, leading to increased free local anesthetic, and (3) pregnancy hormones. The latter is the most likely explanation, based on animal studies. An increased sensitivity to bupivacaine in isolated nerve fibers has been demonstrated (Fig. 1-4).[25]

It is possible that progesterone or one of its active metabolites is responsible for the observed increased sensitivity of the peripheral nervous system to anesthetics in parturients. This increased sensitivity was also observed in nerves from oophorectomized rabbits treated chronically with exogenous progesterone.[26] Interestingly, this phenomenon was not observed following acute exposure to progesterone.[27] In humans, enhanced sensitivity of peripheral nerves to local anesthetic has also been documented.[28]

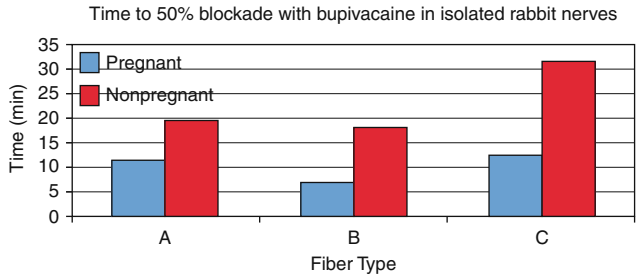

Figure 1–4. Increased sensitivity in nerves in pregnant vs. nonpregnant rabbits. (Data from Datta et al.[25])

Clinical Implications

Even though the exact mechanism of the increased sensitivity of the central nervous system and peripheral nervous system to general and local anesthetics is not known, in general, it is prudent to reduce the dose of anesthetics in pregnant women, at least on initial dosing.

Because of a paucity of data and uncertainty regarding the actual mechanisms underlying enhanced local anesthetic sensitivity in pregnancy, it is not known when these changes revert to their nonpregnant state. Spinal anesthetic sensitivity appears normal 24–48 h postpartum.

Changes in the Endocrine System

Thyroid-binding globulin is increased in pregnancy, but free T_3 and T_4 are normal. Adrenal cortical hyperplasia leads to increases in both free and total cortisol in pregnancy. Fasting blood sugar is lower in pregnant than nonpregnant women, but tolerance to a glucose load may be somewhat impaired due to the actions of placental lactogen, producing a mild diabetogenic state. Occasionally, this progresses to gestational diabetes. Glucose responses return to normal promptly after delivery of the placenta.

Changes in the Musculoskeletal System

The hormone relaxin is responsible for both the generalized ligamentous relaxation and the softening of collagenous tissues. The lumbar spine demonstrates exaggerated lordosis, possibly complicating regional anesthesia. Stretching of the lateral femoral cutaneous nerve can occur, leading to sensory loss in the lateral thigh (meralgia paresthetica). This must be differentiated from neural injury due to childbirth or anesthesia. In addition, back pain frequently accompanies late pregnancy, and pregnant women must be counseled against relating this to regional anesthesia.

Changes in the Dermatological System

Hyperpigmentation of certain parts of the body such as the face, neck, and midline of the abdomen is not uncommon during pregnancy. Melanocyte-stimulating hormone is responsible for this change.

Changes in Mammary Tissue

Enlargement of the breasts is typical and may complicate use of a conventional laryngoscope during induction of general anesthesia. A short-handled laryngoscope may facilitate easier instrumentation of the airway.[29]

Changes in the Ocular System

Intraocular pressure has been shown to decrease during pregnancy; this is related to (1) increased progesterone levels, (2) the presence of relaxin, and (3) decreased production of aqueous humor due to increased secretion of human chorionic gonadotropin. Changes in intraocular pressure in parturients may produce visual disturbances as well as contact lens intolerance.

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2
Local Anesthetic Pharmacology

Local anesthetics are the most common and important drugs in obstetric anesthesia; hence an adequate knowledge of these chemical agents is absolutely essential.

Chemistry

Chemically, local anesthetics are classied as amino-esters or amino-amides (Fig. 2-1). All clinically used local anesthetics (except cocaine) link a substituted aromatic ring via an ester or amide bridge and an intermediate alkyl chain to a tertiary amine. Commercially, most are packaged as hydrochloride salt, protonating the amino group to improve aqueous solubility.

Amino-esters undergo hydrolysis by plasma cholinesterase (pseudo-cholinesterase) to derivatives of para-aminobenzoic

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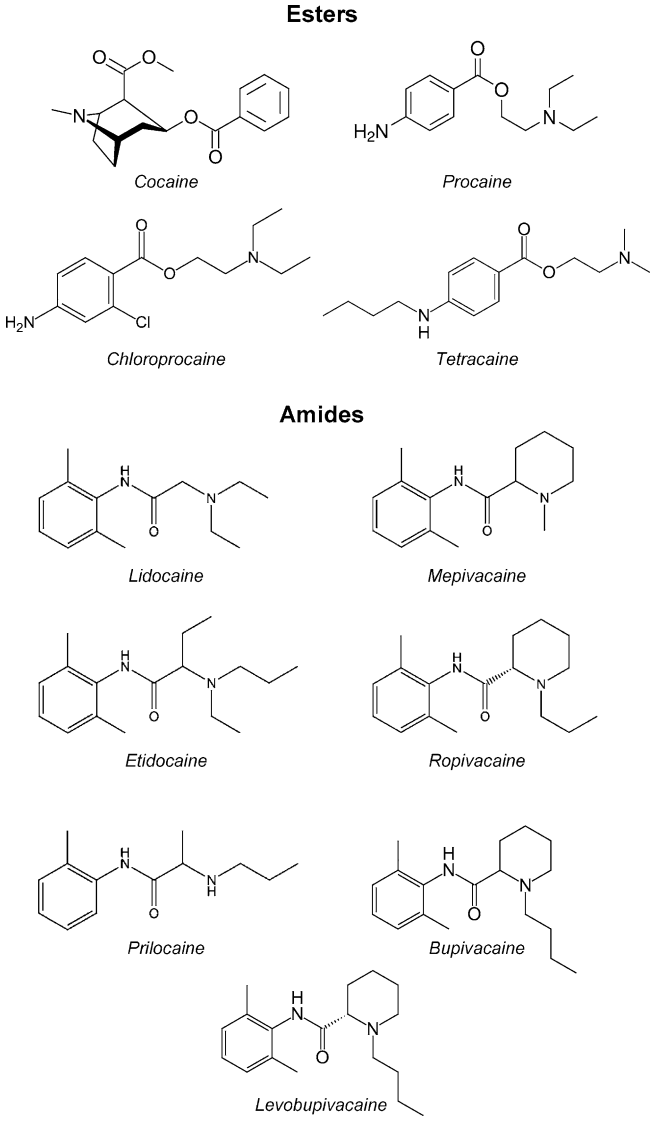

Figure 2–1. Local anesthetics, esters and amides with chemical structures.

acid, which is a known allergen. Hence allergic reactions to amino-esters are not unusual. Conversely, amino-amides are metabolized by the liver to a variety of products with very low potential of triggering allergic reactions.

All local anesthetics except lidocaine contain a chiral carbon atom and thus exist as two enantiomers. Conventional preparations are racemic mixtures, but the development of techniques for bulk separation of optical isomers has led to the development of levobupivacaine and ropivacaine, which are marketed as pure left-handed ("L" or "S") forms.

Physicochemical Properties

The physicochemical properties of local anesthetics correlate with some of their clinical properties (Table 2-1). *Lipid solubility* correlates with the potency of the local anesthetic. This effect is also seen with general anesthetics (the Meyer–Overton observation) and is sometimes attributed to easier passage through the lipid membranes of nerve cells by more lipophilic local anesthetics. More modern views of this observation suggest that it is the perineural lipid-rich tissues which actually form a depot of drug, enhancing continued blockade and thus clinical potency.

Protein binding correlates with the duration of action of local anesthetics. Local anesthetic is bound to two principal sites in plasma: (1) the high-affinity but low-capacity α_1-acid glycoprotein and (2) low-affinity, high-capacity albumin. Although classically taught, this association is not thought to be causal. Plasma protein binding is closely related to lipophilicity, which actually is more responsible for long duration of action.

The p*K*a of local anesthetics correlates to some degree with the speed of onset of neural blockade. p*K*a is defined as the pH where 50% of the local anesthetic will remain in uncharged form and 50% will exist in charged form. Agents with p*K*a closer to the body's pH will be less likely to be protonated and therefore exist more prevalently in the uncharged form (Table 2-1). This form is less polar and more easily able to diffuse across the nerve membrane, perhaps explaining a

Table 2–1. Properties of Local Anesthetics

Anesthetic	Lipid Solubility	Protein Binding (%)	p*Ka* (Unionized Fraction pH 7.4)	Molecular Weight	Potency	Speed of Onset	Duration of Action	UV/MV ratio
Chloroprocaine	0.14	~0	8.7 (5%)	271	Low	Very rapid	Short	~0
Procaine	0.02	6	8.9 (3%)	236	Low	Rapid	Short	N/A
Lidocaine	2.9	64	7.7 (35%)	234	Medium	Rapid	Medium	0.5–0.7
Mepivacaine	0.8	78	7.6 (39%)	246	Medium	Medium	Medium	0.7–0.8
Bupivacaine	8.2	96	8.1 (15%)	288	High	Slow	Long	0.2–0.4
Ropivacaine	8.0	92–94	8.1 (15%)	274	High	Slow	Long	0.2

Lipid solubility: Heptanol or octanol/buffer partition ratio; UV/MV ratio=ratio of concentration in umbilical vein to maternal vein; total concentration, not free drug concentration, is shown in the table (see text for details); N/A = not available.

more rapid onset of blockade. However, the astute reader will note that this mechanism is essentially the same as that asserted for lipid solubility, so the in vivo importance of this action is unclear. Indeed, chloroprocaine, with a p*K*a of 8.7, has the fastest onset of action in clinical practice among all local anesthetics for epidural blockade. Moreover, although the uncharged form is important for diffusion across the nerve membrane, it is believed that the charged form ultimately binds with the sodium channels intracellularly. Hence both forms of the local anesthetic are important for neural blockade.

Some local anesthetics possess *intrinsic vasoactive properties*. Lidocaine produces modest vasodilation in low concentrations, possibly reducing its potency in vivo by increasing vascular uptake. Conversely, ropivacaine has been found to have dose-dependent vasoconstrictive activity,[1] which might increase its duration of action, especially after local infiltration.

Passage of local anesthetics across the placenta is influenced by the physicochemical properties of the drugs. All local anesthetics are relatively small molecules, and therefore molecular weight does not affect their transport. Lipid solubility and degree of nonionization will affect the proportion of maternal venous concentration that exists in the fetal blood, because both enhance passage across the lipid membranes in the placenta (Table 2-1). However, more recent evidence suggests that free drug concentrations for all local anesthetics are in equilibrium across the placenta and in maternal and fetal blood, so the greater protein binding in maternal blood does not necessarily confer a safety advantage to the fetus.

Other Factors Affecting Local Anesthetic Activity

Besides intrinsic physicochemical properties, a number of clinically modifiable factors have a major effect on the degree of neural blockade achieved with local anesthetics.

Volume and Concentration

The total dose (mass or mg) of local anesthetic will ultimately dictate the onset, quality, and duration of the block. In

general, increased doses of the agents speed onset and lengthen duration of the block. For example, increasing the concentration of bupivacaine from 0.125% to 0.5% while maintaining constant volume improved the onset, quality, and duration (but not dermatomal spread) of the block.[2] Volume, concentration, and dose, however, are intimately related, because dose = volume × concentration. Therefore, changing one parameter necessarily changes the others, complicating the study of one feature in isolation. Clinically, volume of drug has a profound effect on the spread and quality of epidurally administered local anesthetics, whereas total dose seems most important in spinal anesthesia.

Addition of Vasoconstrictor Agents

Epinephrine is frequently used with local anesthetics to improve the quality and duration of analgesia. Because of the vasoconstriction produced by epinephrine more local anesthetic will be available for neural blockade because of less absorption through vascular beds. Norepinephrine and phenylephrine have also been used for prolonging blockade, though they are much less popular. Addition of epinephrine will also decrease the peak plasma concentrations of certain local anesthetics, including mepivacaine and lidocaine. Epinephrine is usually added to epidural lidocaine or bupivacaine at concentrations of 1.7–5 μg/ml, or 1:600,000 to 1:200,000 (the latter is also the commercially available concentration). This lowers the median effective concentration of local anesthetic by 30%.[3] In addition, the duration of epidural lidocaine and, to a lesser extent, bupivacaine is significantly prolonged by the addition of epinephrine. In spinal anesthesia, by contrast, epinephrine has minimal effects, increasing the duration of motor but not sensory block with lidocaine, and extending sensory block with bupivacaine by just 4–19 min.[4]

Site of Injection

The onset of action of a local anesthetic varies depending on the site of administration. Spinal and subcutaneous routes

are associated with a more rapid onset, whereas epidural and brachial plexus blocks are associated with a slower onset of action.

Bicarbonate

Local anesthetic solutions, particularly those containing epinephrine, are packaged at low pH to increase the shelf life of the agents. Addition of sodium bicarbonate (1 ml of a 1 M solution to 10 ml local anesthetic) will increase the pH of these solutions and thus the percentage of the nonionized or uncharged form, which is important for diffusion through the nerve membrane. Speed of onset and quality of the block are both improved with this maneuver. Addition of bicarbonate to bupivacaine is not recommended because of the chance of precipitation when the pH rises above 7.7. Laboratory evidence suggests that bicarbonate also enhances local anesthetic activity by other mechanisms distinct from its effect on pH, because its effect is more profound than that induced by equivalent alkalinization with other buffers.[5]

Mixtures of Local Anesthetics: Chloroprocaine and Other Drugs

Historically, combinations of local anesthetics have been used both to shorten the onset of action as well as to improve the quality of the block. A combination of spinal 1% tetracaine and 10% procaine in equal volumes was associated with superior sensory anesthesia when compared with hyperbaric tetracaine (5% dextrose) alone.[6] For epidural administration, it was once hoped that the rapid onset of 2-chloroprocaine and long duration of bupivacaine would produce a desirable combination. However, the use of 2-chloroprocaine shortened the duration of bupivacaine's action.[7] The mechanism of this interaction is unknown but may be related to inhibition of the binding of bupivacaine to membrane receptor sites in the presence of 2-chloroprocaine or its metabolite chloraminobenzoic acid.[8]

The eutectic mixture of local anesthetics (EMLA) is a 1:1 mixture of prilocaine and lidocaine that induces cutaneous

anesthesia through intact skin. Applied in doses of 0.5–1 g under an occlusive dressing, it induces anesthesia for subsequent needle stick in 30–60 min.

Pregnancy

Pregnancy reduces the amounts of local anesthetic needed for both spinal and epidural anesthesia in parturients as compared with age-matched nonpregnant women.[9] The onset of blockade is also faster with the use of spinal, epidural, and peripheral nerve blocks. Although various mechanisms for these observations have been proposed (including influence of mechanical factors in the epidural space and alterations in the central nervous system[10]), the most likely explanation is an effect of progesterone on the sensitivity of nerve fibers themselves.[11]

Temperature

Warming the local anesthetic to a temperature of 100°F has been shown to reduce the onset of epidural anesthesia blockade. A decreased p*K*a due to increased temperature is probably the mechanism.[12]

Toxicity of Local Anesthetics

Local anesthetics can result in systemic toxicity manifest in the CNS or the cardiovascular system, as well as peripheral toxicity manifest as irreversible conduction blockade or other neurological symptoms. Local anesthetics may also cause untoward effects on the fetus.

Systemic Toxicity: CNS

The clinical features of systemic toxicity depend on the blood concentrations of the local anesthetics. In most cases, CNS symptoms will precede cardiovascular derangements. In lower concentrations, the patient may complain of (1) tinnitus, (2) light-headedness, (3) metallic taste, and (4) perioral numbness. With higher concentrations, convulsions and

unconsciousness, followed by respiratory arrest, may ensue. If a large bolus dose of local anesthetic is accidentally injected intravenously the parturient may manifest convulsions as the first sign. This may also occur if the pregnant woman receives large doses of diazepam or midazolam as premedication, because these drugs may mask the subjective symptoms associated with lower blood levels. Respiratory acidosis (increased $PaCO_2$ and low pH) decreases the convulsive threshold and may also increase drug delivery to the brain by increasing cerebral blood flow. Acidosis may also decrease the free plasma concentrations by reducing protein binding. The potency of local anesthetics closely parallels their relative toxic potential: bupivacaine > lidocaine > > chloroprocaine.

Systemic Toxicity: Cardiovascular System

Local anesthetics inhibit cardiac sodium channels and in some cases potassium and calcium channels. However, the heart is highly resistant to toxicity from lidocaine, and indeed seven times the convulsive dose is required to produce cardiovascular collapse with this drug (at plasma concentrations of approximately 25 μg/ml vs. 7–12 μg/ml). Cardiovascular toxicity may result indirectly from respiratory depression, however (at approximately 20 μg/ml). In contrast, high systemic levels of more potent local anesthetics (bupivacaine, etidocaine) produce cardiovascular toxicity at much lower multiples of the convulsive dose. This is due to their pro-arrhythmic effects on the pacemaker and conduction cells in the heart, decreasing the duration of the action potential and the effective refractory period. Thus reentrant-type ventricular dysrhythmias (ventricular tachycardia or fibrillation) may result.

Cardiovascular toxicity of local anesthetics appears significantly more likely with right-handed (R- or D-) isomers of potent lipophilic local anesthetics. This observation led to the development of levobupivacaine and ropivacaine, which are both packaged as pure L- or S-isomers. Levobupivacaine has essentially identical clinical properties as racemic bupivacaine, but is less toxic in both isolated cardiac and intact animal preparations. In human studies, racemic bupivacaine produces more signs of impending cardiovascular toxicity (changes in

the QT interval, decrease in cardiac performance) than does levobupivacaine. Ropivacaine also produces less cardiovascular toxicity in similar preparations and clinical trials. However, ropivacaine is also significantly less potent than bupivacaine; studies comparing the median effective concentration for labor analgesia demonstrate it to be 40% less potent. Nonetheless, even after accounting for this difference, ropivacaine is less toxic. Whether the toxicity difference is clinically relevant in obstetric anesthesia practice, where concentrations used are generally low and large bolus administration is rare, is a matter of some controversy given ropivacaine's much higher cost.[13]

Peripheral Neurotoxicity

Despite decades of clinical experience with local anesthetics for neuraxial block and a paucity of reports of neurotoxicity, over the last two decades evidence has mounted to suggest that under certain circumstances, irreversible conduction blockade may occur with clinical use of certain local anesthetics.

First, 2-chloroprocaine preserved with sodium meta-bisulfite, which was intended for epidural administration, was associated with several cases of cauda equina syndrome (irreversible conduction blockade of L_1 to sacral spinal roots) when unintentionally administered intrathecally. Although somewhat controversial, the mechanism appeared to be related to formation of sulfurous acid in CSF, derived from meta-bisulfite.[14] In in vitro studies, meta-bisulfite and low pH, but not chloroprocaine itself, caused irreversible conduction blockade. However, others have argued exactly the opposite, that bisulfite is in fact *protective* and that chloroprocaine itself is neurotoxic.[15] Fortunately, other preparations of 2-choroprocaine have replaced the bisulfite-preserved form. For some time, the drug was packaged with EDTA; this preparation, however, was associated with significant back pain attributed to chelation of calcium in paraspinous muscles.[16] Most recently, a preservative-free preparation has been marketed in a light-protected bottle. This formulation has been used apparently safely for spinal anesthesia.[17]

Second, 5% hyperbaric lidocaine has caused cases of irreversible blockade, especially when administered in large doses

via a spinal microcatheter. Shortly after the introduction of 27–32 G catheters, which could be placed through 25 G or 26 G spinal needles, case reports of cauda equina syndrome began to surface.[18] Subsequent laboratory investigation demonstrated that lidocaine caused concentration-dependent neurotoxicity when applied directly to nerves.[19] Other studies implicated pooling of hyperbaric local anesthetic in the posterior lumbosacral spinal canal (where the cauda equina fibers lay in the supine patient) when administered by the slow laminar flow caused by the narrow-gauge catheters.[20] Though the catheters were withdrawn from the market, reintroduction in the near future appears likely, given extensive European experience and a recent multicenter North American randomized trial which demonstrated comparable safety and efficacy of rationally dosed microcatheters compared to conventional epidural catheters.[21]

Finally, a milder form of apparent toxicity following hyperbaric spinal lidocaine has been termed transient neurologic symptoms (TNS). Other terms for the same syndrome include transient radicular irritation (TRI) and post-spinal pain syndrome (PSPS). These terms describe the development of short-lived back, buttock, or thigh pain unaccompanied by objective sensory or motor deficits, following spinal anesthesia. The onset of symptoms is typically within the first day, duration usually less than 5 days, and intensity moderate to severe (average VAS 6/10). NSAIDs provide the best available symptomatic treatment. Epidemiologic surveys and RCTs suggest it is far more common with lidocaine than other local anesthetics, is more likely after procedures in the lithotomy position, and probably more common in ambulatory surgical cases.[22] Unlike the more severe cauda equina syndrome, concentration and dose of lidocaine are not risk factors. Moreover, experiments in volunteers suggest there is no objective neurotoxicity.[23] Fortunately, the incidence in pregnancy appears to be much lower than in general surgical patients.[24] Nonetheless, we prefer the use of mepivacaine 1.5%, made hyperbaric by the addition of 10% dextrose, for outpatient spinal anesthesia in pregnant patients (e.g., for cervical cerclage placement) due to the low incidence of TNS even in general surgical patients.[25]

Adverse Effects on the Fetus

Local anesthetics administered in high concentrations can cause uterine artery constriction in isolated vessels. This observation grew from clinical reports of fetal bradycardia following paracervical block for labor analgesia, during which large doses of concentrated drug are deposited near the uterine arteries. In modern clinical use for epidural and spinal anesthesia, local anesthetics do not alter uterine or umbilical blood flow. Conversely, there is some evidence that even clinically encountered concentrations of local anesthetic may adversely affect blood flow distribution within the asphyxiated fetus.[26] In preterm pregnant ewes, lidocaine interfered with the normal compensatory shunting of blood flow to the heart, brain, and adrenal glands during asphyxia. This effect was less pronounced in term fetuses or when bupivacaine was administered. The applicability of these results to human patients with possibly compromised fetuses is far from clear. However, some clinical evidence supports the use of chloroprocaine in preference to other local anesthetics in such settings.[27]

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3
Perinatal Pharmacology

Perinatal pharmacology involves the three most important participants in pregnancy: the mother, the placenta, and the fetus (Fig. 3-1). Virtually all drugs administered to the mother can traverse the placenta and appear in the fetal circulation to some extent. Hence an appreciation of perinatal pharmacology is important for the safe conduct of obstetric anesthesia.

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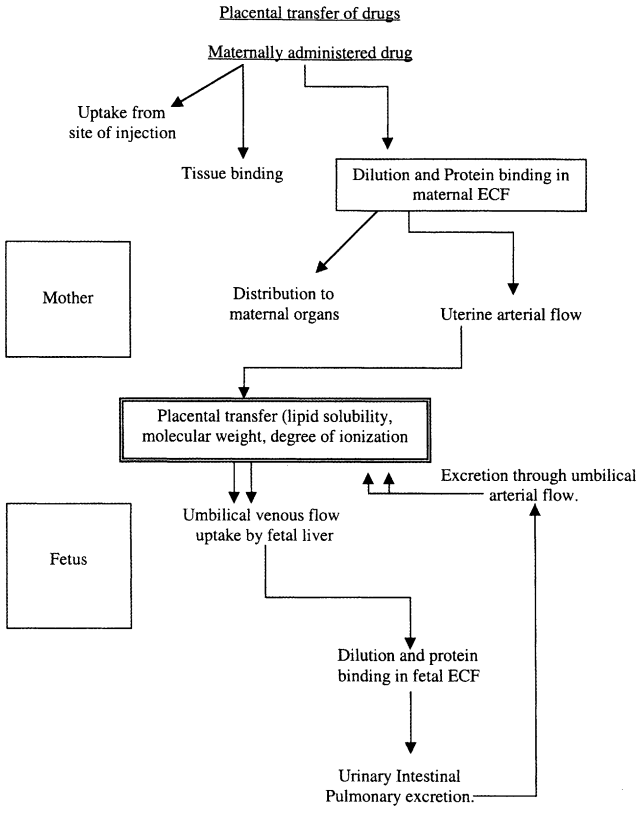

Figure 3–1. Drug disposition in the mother, placenta, and fetus.

General Principles

Maternal drug administration can affect the fetus in two ways: (1) a direct fetal effect, via transplacental passage into the fetal circulation, and (2) an indirect effect, by affecting uteroplacental blood flow. The latter is discussed in Chapter 5.

Substances in the maternal circulation can cross the placenta by one of four mechanisms. The majority of substances are subject to *passive diffusion*, in which the compound flows across lipid membranes down a concentration gradient. The degree of flow is proportional to the concentration difference between the maternal and fetal circulations, and is affected by a number of factors discussed in detail below. Some substances are subject to *facilitated diffusion*, in which a carrier protein in the lipid membrane aids passage of the substance, again down a concentration gradient. Glucose crosses from the maternal to fetal circulation in this way. *Active transport* refers to an energy-requiring process in which a transporter molecule moves the substance, often against a concentration gradient (i.e., from lower to higher concentration). A variant of this process is co-transport, in which the movement of one substance is linked to the movement of another, also in an energy-requiring step. Amino acids appear to cross from the maternal to fetal circulation in this way, co-transported with sodium. Finally, some large molecules, such as immunoglobulins, are transferred via *pinocytosis*, in which invaginations of cell membranes surround the molecule to form a vesicle that subsequently fuses with a cell in the other circulation and releases the molecules.

For substances subject to passive diffusion, the movement of the compound across the placenta can be described by the diffusion equation:

$$Q/t = \frac{KA(C_m - C_f)}{D} \tag{3-1}$$

where Q/t is the quantity of the drug transferred in a unit of time; K is a diffusion constant; A is the total diffusion area of the placenta; C_m and C_f are the maternal and fetal concentration of free drugs, respectively; and D is the diffusion distance across the placenta. Factors that alter the amount present in the fetal circulation include those that affect the maternal concentration (C_m), factors related to the substance and its interaction with the placenta (K, A, and D), and factors related to fetal handling of the substance (C_f).

The Mother

Site of Administration

The maternal plasma concentration of any agent will depend upon the site of administration as well as the amount of agent administered. In the case of local anesthetics, the highest to lowest maternal plasma concentration will be achieved by the following routes of administration: intravenous > paracervical > caudal epidural > lumbar epidural > intramuscular > subarachnoid block.[1]

Addition of Epinephrine

Epinephrine can slow the absorption of local anesthetics injected subcutaneously or epidurally. It has been shown to reduce the peak maternal plasma concentration of lidocaine and mepivacaine.[1] However, epinephrine has an insignificant effect on peak concentrations of bupivacaine.

Maternal Volume of Distribution and Clearance

The volume of distribution for many drugs is increased in pregnancy, likely due to an increase in plasma volume and body fat. However, clearance of some drugs may be decreased (thiopental), unchanged (succinylcholine), or increased (vecuronium). Because sensitivity to many anesthetic drugs is increased in pregnancy (inhalation anesthetics, thiopental, vecuronium, local anesthetics), smaller doses may be administered to achieve the same clinical effect as in nonpregnant women, reducing the maternal blood concentration attained.

Ester drugs such as 2-chloroprocaine, succinylcholine, and remifentanil are metabolized by plasma cholinesterases; hence the maternal plasma half-life of these drugs is very short, and less drug will ultimately reach the fetus. Conversely, some drugs have long-lived metabolites which can reach the fetus. For example, normeperidine, a metabolite of meperidine, is twice as toxic as the parent compound but only half as analgesic. This metabolite is cleared only slowly by the fetus.[2,3] Infants born

more than 4 h after maternal meperidine may be depressed due to accumulation of normeperidine in their tissues.

Uteroplacental Blood Flow

Maternal blood must enter the uteroplacental circulation for substances to cross the placenta into the fetus. Factors that increase or decrease blood flow may alter transport of various substances, particularly those with flow-limited, as opposed to diffusion-limited transport.[4] In addition, during uterine contraction, when blood flow is reduced or halted, transport will be sharply reduced; if maternal drug concentrations decline during the interval of reduced flow, overall transport may be reduced.

Maternal Protein Binding

Plasma protein binding may be important for placental transfer. It is the free drug, not the protein-bound fraction, that is in equilibrium across the placenta. However, protein binding differs markedly among drugs, and fetal protein binding is only about 50% of that in the mother. Therefore, highly protein-bound drugs (such as bupivacaine) will exist in much higher total concentrations in the mother than the fetus, as measured by the fetal:maternal plasma ratio or umbilical vein to maternal vein (UV/MV) concentration ratio. The effect of protein binding on the rate of transfer of drugs is less clear. It appears that free and bound drugs are in rapid equilibrium, so such binding should have a minimal effect.

Maternal pH and Drug pKa

Highly charged drugs cross the lipid membranes of the placenta inefficiently. Therefore, ionizable drugs with a p*K*a close to the body's pH of 7.4 will exist in a greater fraction in the nonionized form in maternal blood, and this will be associated with higher placental transfer. For example, mepivacaine with a p*K*a of 7.6 will cross the placenta in higher amounts when compared with bupivacaine with a p*K*a of 8.1 or the closely related ropivacaine and levobupivacaine. Conversely, maternal pH changes due to metabolic or respiratory disorders, or due

to hyperventilation-induced alkalosis, may alter the available fraction of a drug available for placental transfer.

The Placenta

Area of Transfer and Diffusion Distance

The rate of drug transfer depends upon the effective area of transfer. The maternal part of the placenta contains 180–320 spiral arteries. The functional unit of the placenta is the "placentone," which is supplied by a single spiral artery. It has been speculated that placental abnormalities, such as cocaine-induced edema, chorioamnionitis, or preeclampsia, may alter the diffusion distance (see Equation 3-1). The clinical significance of these changes is unclear.

Molecular Weight and Spatial Configuration of Drugs

Drugs with a molecular weight less than 500 daltons (Da) will freely cross the placenta. Drugs above 500 Da will cross with difficulty, and most drugs above 1,000 Da will not cross the placenta in appreciable amounts.[5] Most clinically useful drugs will cross the placenta because of their low molecular weight. However, heparin and protamine do not cross the placenta because of their large molecular weight (MW). Highly ionized drugs generally cross the placenta less easily. However, there are exceptions to these rules, and large drugs (e.g., vancomycin, MW = 1449 Da) and charged drugs (e.g., ampicillin) do sometimes cross the placenta readily.[6]

Protein Binding and Lipid Solubility of Drugs

Drugs bound to plasma protein were previously thought to cross the placenta with great difficulty (as inferred by the fetal:maternal ratio). However, more recent data suggest these drugs rapidly equilibrate with the free form, and protein binding may not appreciably affect placental transfer.[5] Lipid solubility eases the transfer of drugs through the placenta. Highly lipid-soluble drugs, such as barbiturates, can reach the

fetus in large amounts after easy placental transfer. However, some drugs with very high lipophilicity such as sufentanil may become bound in the lipid membranes of the placenta itself, reducing total transfer to the fetus.[7]

Metabolism of Drugs

The placenta can manufacture and excrete specific enzymes, including many subtypes of the cytochrome P450 system, that will destroy maternally administered drugs.[8] A common clinically relevant example is prednisone, which is metabolized by the placenta and therefore appears in minute concentrations in the fetus.

The Fetus

Fetal uptake, distribution, and metabolism and elimination will ultimately be responsible for the fetal drug concentration and its effect on the fetus. Once drugs reach the fetus, several important factors will determine the free umbilical artery concentration of drugs.

Uptake

Fetal uptake of drugs will depend on protein binding, lipid solubility, and the p*K*a of the drugs. Because of lesser amount of total protein in the fetus, plasma protein-binding capacity in the fetus is less than in the mother. As noted, total plasma concentration will be lower than in the mother for highly protein-bound drugs, but free drug concentrations will be approximately equal at equilibrium. Highly lipid-soluble drugs (e.g., bupivacaine) will redistribute within the fetus as they do in the adult. Finally, and most importantly, fetal pH can play a significant role in determining the amount of drug in the fetus at equilibrium. Normal fetal pH varies between 7.32 and 7.38, whereas maternal pH varies between 7.38 and 7.42. In a normal situation, maternal fetal transfer of the drug will depend mostly on the concentration gradient. However, if the fetus is acidemic, then un-ionized drugs from the mother will cross the placenta and be preferentially protonated to the ionized (charged) form. Because the ionized form crosses the placenta

less efficiently, the *ionized form of drugs will get "trapped" and accumulate in the fetus. This phenomenon has been described as "ion trapping" and to avoid it chloroprocaine is recommended for epidural anesthesia when the fetus is suspected to be acidotic.*[9,10]

Distribution

Drugs enter the fetal circulation via the umbilical vein and redistribute within the fetus as they do in the adult (Fig. 3-2). The umbilical arterial concentration of drugs will frequently be lower than that of the umbilical vein, and it may better reflect the concentration in critical organs such as the brain and heart.

Fetal Liver

The umbilical vein blood from the placenta either reaches the liver or flows through the ductus venosus. The left lobe of the liver is transfused by umbilical venous blood, whereas the right lobe is perfused by portal venous blood. Because UV blood-containing drugs will pass through the liver before entering the systemic circulation, the fetal liver helps in extracting substantial amounts of drug entering the fetus and thereby helps in protecting the fetal brain. For example, thiopental administered intravenously to the mother is taken up by the fetal liver in a significant amount.[11]

Progressive Dilution of Umbilical Vein in Blood Concentration

Umbilical vein blood passing through either the fetal liver or the ductus venosus will ultimately be diluted by the blood received from the lower extremities or gastrointestinal tract.

Extensive Right-to-Left Shunt of the Fetal Circulation

After reaching the fetal heart, approximately 57% of fetal cardiac output returns to the placenta without perfusing fetal

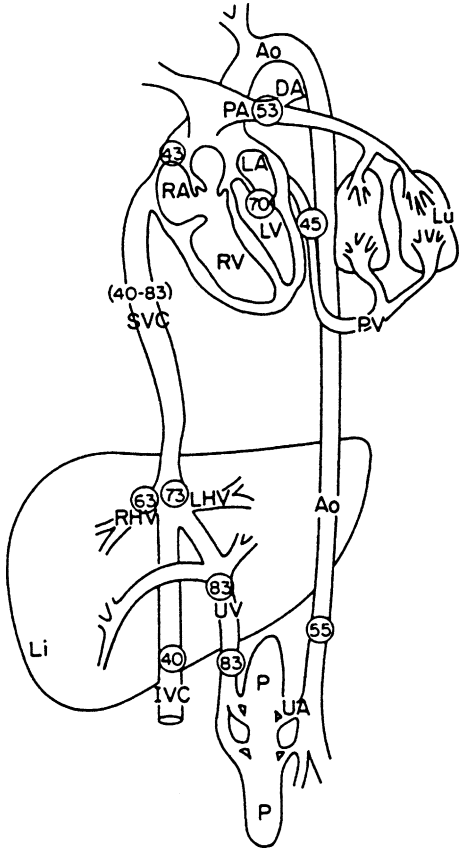

Figure 3–2. Fetal circulation (numbers indicate percent saturation). IVC = inferior vena cava; P = placenta; Li = liver; RHV, LHV = right and left hepatic veins; SVC = superior vena cava; RA, LA = right and left atria; DA = ductus arteriosus; PA = pulmonary artery; Ao = aorta; Lu = lung; DV = ductus venosus; PV = pulmonary vein; UV = umbilical vein; UA = umbilical artery. (From Martin.[12])

tissues. This is related to extensive shunting of the fetal circulation via the foramen ovale of the heart as well as the ductus arteriosus. This mechanism leads to diminished exposure of the fetal brain to circulating drugs.

Summary

Clinically, the above mechanisms help explain why after thiopental administration to the mother for cesarean section, a vigorous crying infant may be delivered from a sleeping mother. It is also reassuring that the fetus may be unaffected when lower doses of maternal sedatives are required during regional anesthesia for labor or operative delivery.

In summary, the majority of maternally administered drugs will cross the placenta and reach the fetus, but because of the unique fetal circulation, reduced amounts of the drugs will reach the fetal brain and myocardium.

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4
Drug Interactions and Obstetric Anesthesia

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Drugs Used for Maternal Indications

Antibiotics

Often, parturients may receive antibiotics for various disease processes. This is particularly observed in high risk management labor and delivery units. *Most of the antibiotics will prolong the effect of nondepolarizing muscle relaxants, but prolongation of depolarizing muscle relaxants has also been observed* (Table 4-1).[1,2] The table cites the example of d-tubocurarine; however, the duration of action of presently used muscle relaxants including vecuronium and rocuronium are also prolonged by antibiotics.[3–5] The mechanism of this phenomenon is unknown. Antagonism of this action by neostigmine and pyridostigmine is found to be unpredictable; however, neuromuscular blockade from antibiotics could be reversed predictably by 4-aminopyridine.[2] An interesting observation made in rats that may have clinical bearing is that the neuromuscular block produced by a combination of neuromuscular-blocking drugs and antibiotics could be prolonged in the presence of local anesthetic lidocaine.[6]

Antiepileptic Drugs

Parturients may be taking antiepileptic drugs when they arrive in the hospital for labor and delivery. The common antiepileptic drugs at the present time include phenytoin, phenobarbital, benzodiazepines, and valproic acid. *The pharmacokinetics of most of the antiepileptic drugs is altered during pregnancy. Parturients need higher amounts of antiepileptic drugs because of increased volume of distribution; hence measurement of the plasma concentration is important.* Most of

Table 4–1. Interaction of Antibiotics, Muscle Relaxants, Neostigmine, and Calcium

	Neuromuscular Block from Antibiotic Alone Antagonized by		Increase in Neuromuscular Block of		Neuromuscular Block from Antibiotic and *d*-Tubocurarine Antagonized by	
	Neostigmine	Calcium	*d*-Tubocurarine	Succinylcholine	Neostigmine	Calcium
Neomycin	Sometimes	Sometimes	Yes	Yes	Usually	Usually
Streptomycin	Sometimes	Sometimes	Yes	Yes	Usually	Usually
Gentamicin	Sometimes	Yes†	Yes	‡	Sometimes	Yes†
Kanamycin	Sometimes	Sometimes	Yes	Yes	Sometimes	Sometimes
Paromomycin	Yes†	Yes†	Yes	‡	Yes†	Yes†
Viomycin	Yes†	Yes†	Yes	‡	Yes†	Yes†
Polymyxin A	No	No	Yes	‡	No	No
Polymyxin B	No§	No	Yes	Yes	No§	No
Colistin	No	Sometimes	Yes	Yes	No	Sometimes
Tetracycline	No	‡	Yes	No	Partially	Partially
Lincomycin	Partially	Partially	Yes	‡	Partially	Partially
Clindamycin	Partially	Partially	Yes	‡	Partially	Partially

† In spite of this, difficulty with antagonizing the block from these antibiotics is still likely to occur.
‡ Not studied.
§Block augmented by neostigmine.
From Smith and Corbascio.[2] Used with permission.

these drugs are metabolized in the liver and thus can interfere with the biotransformation of other drugs. The duration of action of the drugs, which are mainly metabolized by the liver, can be prolonged in parturients who are receiving antiepileptic drugs. *These drugs also cross the placenta and can thus interfere with the synthesis of vitamin K-dependent clotting factors in the fetal liver. Hence, careful observation of the neonate is essential.* Regional anesthesia should be the anesthetic technique of choice because there is evidence that a local anesthetic like lidocaine can be an effective anticonvulsant in therapeutic doses.[7] *If general anesthesia is indicated, the use of enflurane should be avoided because of its epileptogenic property.*[8]

Enzyme Induction

Enzyme induction is an adaptive response associated with accumulation of specific mRNAs and increased expression of the associated enzyme system. *Oxidative metabolism is catalyzed by the P450 enzyme system.* P450 enzymes have been grouped into three families: CYP_1, CYP_2, and CYP_3. Several medications selectively induce specific families of the P450 enzyme system. Rifampicin decreased concentration of midazolam; its elimination half-life was also reduced.[9]

Sympatholytic and Sympathomimetic Drugs

Pregnant women may use both sympathetic nervous system agonist and antagonist drugs for either therapeutic or recreational reasons.

Sympatholytic Drugs

Sympathetic nervous system antagonists are used for the treatment of hypertension; α-methyldopa, reserpine, and guanethidine have been used in parturients. *Depletion of norepinephrine is possible in such a situation, and indirect-acting agonists like ephedrine may be ineffective following hypotension.*[10] Direct-acting agonists like phenylephrine may be indicated in such circumstances. Besides these antagonist agents, β-receptor antagonist drugs like propranolol can be

used for therapeutic reasons. *If the parturient is taking propranolol, medications that increase airway resistance, such as large doses of morphine or prostaglandin F_{2a} (PCF_{2a}) (Prostin), should be used cautiously.* Calcium channel blockers with negative inotropic effects can exaggerate the depressant effect of propranolol. *Propranolol will cross the placenta and can cause fetal bradycardia and hypoglycemia*. Autonomic ganglionic blocking drugs like trimethaphan camsylate (Arfonad) are used occasionally to treat hypertension. Because this drug is destroyed by cholinesterase, which is also responsible for the metabolism of succinylcholine, a prolonged neuromuscular block has been described following the use of trimetaphan and succinylcholine.[11] A few words of caution must be mentioned in using beta-blockers such as esmolol. *Severe fetal bradycardia has been described when esmolol was given to the mother.* The proposed mechanisms include (1) large placental transfer and (2) more beta-specific medications have unrestricted alpha constriction of the uterine blood vessels.

Labetalol (alpha and beta-blocker) has become a popular choice for the treatment of hypertension during pregnancy or in parturients with preeclampsia. The short-term effect of 0.8 mg/kg of an intravenous bolus of labetalol on maternal and fetal hemodynamics was investigated in 10 women with pregnancy-induced hypertension.[12] The maximum effect occurred within 35 min after labetalol administration. The mean arterial pressure decreased by 18% and there was a slight decrease in maternal heart rate. As to flow velocity waveforms, no significant change was found in mean systolic/diastolic (S/D) ratio of the uterine artery, umbilical artery, or fetal middle cerebral artery. However, a marked reduction in blood pressure can decrease uterine artery S/D ratio. After administration of regional anesthesia, excessive hypotension should be avoided to maintain uterine blood flow. Before general anesthesia smaller doses of labetalol 5–10 mg intravenously should be used to decrease detrimental effects to the fetus.[13]

Sympathomimetic Drugs

Two drugs in this group that are used recreationally are worth mentioning:

1. *Amphetamine* is a central nervous system (CNS) stimulant. A new smoked form, "ice," that produces a "high" of long duration is popular in Hawaii and on the West Coast of the United States. The minimum alveolar concentration is increased in parturients who are addicted to amphetamines. Higher doses of narcotics and inhalational anesthetics may be needed for general anesthesia.[14] Vasopressors, both direct and indirect acting, should be used carefully for the treatment of hypotension.
2. *Cocaine* is one of the commonly used recreational agents at the present time. *It blocks the presynaptic uptake of norepinephrine, serotonin, and dopamine.* Chronic use will decrease α_2-adrenergic- and presynaptic cholinergic mediated norepinephrine release.[15] Cocaine is metabolized by cholinesterase and can affect the metabolism of 2-chloroprocaine. Ketamine or excessive catecholamines can cause severe hypertension and myocardial infarction. Tachycardia following cocaine use should be treated with labetalol because pure β-adrenergic agents will have unopposed α-adrenergic activity with associated hypertension.[16] Calcium channel blockers will also have unopposed action. Decreased pseudocholinesterase levels may prolong the duration of action of succinylcholine.

Antiasthmatic Drugs

Xanthine Derivatives

Xanthine derivatives such as theophylline and aminophylline may be associated with different drug interactions. Cimetidine has been observed to slow down the elimination of theophylline.[17] If general anesthesia is indicated, ketamine should be used carefully because the combination of ketamine and aminophylline can cause significant lowering of the seizure threshold.[18] Methylxanthines are associated with the release of endogenous catecholamines. In the past this was of importance when halothane was used as inhalational anesthetic during general anesthesia as this can induce dysrhythmias. This is further exaggerated if the parturient receives ephedrine or epinephrine at the same time.[19] Theophylline can antagonize

a nondepolarizing muscle-relaxant block. This is more likely to occur with pancuronium than vecuronium.[20] The mechanism is unknown. Pancuronium should be used cautiously because of the possibility of supraventricular tachycardia.[21]

Corticosteroids

Corticosteroids have been observed to alter the disposition of theophylline. The intravenous administration of large doses of corticosteroids was associated with a twofold increase in serum levels of theophylline in patients who were receiving a theophylline infusion.[22]

Histamine H_2 Receptor Blockers

The use of H_2 receptor blockers has become a common practice before cesarean section. Both cimetidine and ranitidine have been used as premedicant agents. Cimetidine binds to the hepatic microsomal cytochrome P450 system. Cimetidine as well as ranitidine significantly decrease hepatic blood flow and thus can decrease hepatic clearance of various drugs. Chronic cimetidine use will decrease clearance as well as the metabolism of drugs like theophylline, benzodiazepines, morphine, lidocaine, and propranolol.[23–25] Ranitidine does not bind with cytochrome P450 and is more potent than cimetidine; hence drug interactions with ranitidine are extremely rare.

Psychotropic Agents

A broad range of antipsychotic drugs are available at the present time, and these drugs may be associated with multiple complex drug interactions. Three commonly used groups of drugs include phenothiazine, thioxanthenes, and butyrophenones. Antipsychotic drugs are associated with elevation of serum prolactin levels and blocking of dopaminergic receptors.[26]

Phenothiazine, Thioxanthenes, and Butyrophenones

Effect on Narcotics. Most of the antipsychotic drugs will enhance the effect of narcotic analgesics. This might have additive and/or synergistic effects.[27] One has to reduce the dose of narcotics if the patient is taking antipsychotic drugs.

Central Nervous System Depressants. Antipsychotic drugs also exert an increased effect on sedative and hypnotic drugs. A study showed that chlorpromazine decreased the thiopental requirement as well as prolonged postoperative recovery following thiopental use.[28]

Sympathomimetic Drugs. Antipsychotic drugs can block the pressor effects of norepinephrine and other α-adrenergic agonist drugs.[29] Hence, higher doses of vasopressors may be necessary to treat hypotension in these cases. Selective α-adrenergic-blocking effects of these drugs may exaggerate the effects of drugs with β-agonist activity (propranolol).[30]

Anticholinergic Drugs. Some antipsychotic drugs like chlorpromazine and thioridazine do exert active anticholinergic effects: hence one has to be careful while administering anticholinergic premedications.[31]

Inhalation Anesthetics. There may be higher incidence of hypotension when inhalational anesthetics are used in women taking antipsychotic drugs. Therefore, caution has to be exercised while administering general anesthetic in these patients.

Regional Anesthesia. A higher incidence of hypotension has been described in women receiving chlorpromazine. Adequate volume replacement and active treatment of hypotension are important.[32] Direct-acting α-agonists like phenylephrine may be necessary for the treatment of hypotension.

Other popular psychotropic drugs outside the three main groups (phenothiazine, thioxanthenes, and butyrophenones) are tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs), lithium, and serotonin reuptake inhibitors (SSRIs).

Tricyclic Antidepressants

The mechanisms of action include blocking the uptake of norepinephrine, serotonin, or dopamine into presynaptic nerve endings, thus increasing central and peripheral adrenergic

tone. Tricyclic antidepressants also possess a strong anticholinergic effect. Drug interactions with tricyclic antidepressants are complex, and the obstetric anesthesiologist must be aware of the problems. *Tricyclic antidepressants heighten the pressor response of direct-acting vasoactive drugs such as norepinephrine, epinephrine, or phenylephrine.*[33,34] *Hence, local anesthetic solution containing epinephrine should be used cautiously. Ephedrine may not be effective for treating hypotension in this group of women following regional anesthesia. Phenylephrine, in small doses, may be necessary in such circumstances.* Tricyclic antidepressants will also exaggerate the response of anticholinergics and narcotics as well as other sedative and hypnotic drugs (Table 4-2).

Table 4–2. Some Interactions Between Tricyclic Antidepressants and Drugs Used in Anesthesia

Tricyclic Antidepressants	Interaction
Narcotics	↑Analgesia ↑Respiratory depression
Barbiturates	↑Sleep time
Anticholinergics	↑Central activity ↑Peripheral activity
Sympathomimetics	↑Effect of direct-acting agents

From Janowsky et al.[65] Used with permission.

Monoamine Oxidase Inhibitors

These drugs work by inhibiting the enzyme monoamine oxidase. Monoamine oxidase is responsible for the oxidative deamination of serotonin, norepinephrine, and dopamine (Table 4-3); thus their metabolism is disturbed by this group of drugs (MAOIs). These drugs can also inhibit other hepatic microsomal enzymes. Three important drug interactions to consider for parturients receiving MAOI agents are sympathetic amine interactions, narcotic analgesic interactions, and muscle-relaxant interactions. *Indirect-acting sympathomimetic drugs such as amphetamine, methamphetamine, mephentermine, metaraminol, and ephedrine can release excessive amounts of catecholamine and can be associated with*

Table 4–3. Biosynthesis and Metabolism of Catecholamines

Catecholamine		Enzyme	Enzyme Inhibitors
Phenylalanine			
↓	←	Hydroxylase	
Tyrosine			
↓	←	Hydroxylase	←α-methyl-p-tyrosine
DOPA	Rate limiting		
↓	←	Decarboxylase	←α-methyldopa (Aldomet)
Dopamine			
↓	←	β-hydroxylase	←Disulfiram (Antabuse)
Norepinephrine	Rate limiting		
↓	←	*N*-methyltransferase	
Epinephrine			
↓	←	COMT†	←Pyrogallol, Tropolone
Metanephrine			
↓	←	MAO	←MAO inhibitor (Pargyline)
Vanillylmandelic acid			

†COMT = catechol-*O*-methyltransferase.
From Wona and Everett.[66] Used with permission.

severe hypertension in parturients receiving MAOI agents.[34] *Therefore, in women receiving* MAOI *agents, small incremental amounts of a direct-acting vasopressor may be the drug of choice to treat hypotension following regional anesthesia.*[33]

Meperidine's interaction with MAOI agents is complex and can precipitate a hypertensive crisis. Severe respiratory depression, hypotension, and coma have also been described.[35,36]

The mechanisms are not completely clear; however, the hypertensive crisis may be explained by the presence of elevated brain serotonin concentrations in the presence of an MAOI and meperidine because of the inhibition of enzyme metabolism by MAOI agents. Because meperidine is still one of the most common analgesics used for obstetric cases, one has to be very careful in patients receiving concomitant MAOI. Metoclopramide has been observed to potentiate opiate analgesia. The administration of metoclopramide was associated with a reduction in demand of analgesic requirements and a significant reduction in pain scores.[37]

Prolonged apnea following succinylcholine administration has been described in patients receiving MAOI agents. A decrease in plasma cholinesterase content may be responsible for this interaction; since pregnancy also is associated with a decrease in plasma cholinesterase activity, caution is in order.[38]

Lithium Carbonate

Lithium is used for the treatment of recurrent depression. *Interactions of lithium with a few agents used during general anesthesia are important. Lithium can prolong the activity of succinylcholine, pancuronium, and barbiturates.*[39] Lithium rapidly crosses the placenta and can also affect neonates.[40]

Serotonin Reuptake Inhibitors

Serotonin reuptake inhibitors (SSRIs) are another class of drugs in use. Serotonin is an important neurotransmitter as well modulator in both peripheral and central nervous systems. Both selective serotonin receptor agonists and antagonists have been used. Some of these agents have been used for migraine headaches, vascular disorders, neuropathic pain, nausea, and vomiting. However, SSRIs are popular mainly in the area of psychological illness, especially major depression. Important pharmacologic interactions have been observed while treating the women with serotonergic drugs if they are taking serotonin inhibitors (e.g., fluoxetine).

The Serotonin Syndrome. This potentially life-threatening symptom complex has been described with chronic use of SSRIs and interaction with other serotonergic drugs. Clinical features include disorientation, confusion, agitation, restlessness, fever, shivering, diaphoresis, diarrhea, hypertension, tachycardia, ataxia, hyperreflexia, and myoclonus movements. All are related to exaggerated serotonin effects both peripherally and centrally.

Anesthetic Implications. SSRIs are eliminated by hepatic biotransformation involving the cytochrome P450 and its isoenzymes (2DG, 1A2, 2C, 3A4). These medications, as well as some of their metabolites, can inhibit the cytochrome P450 isoenzymes. Thus, plasma concentrations of any drugs that rely on hepatic metabolism and clearance will increase. One should carefully follow any parturient who is on chronic SSRI therapy: (1) preoperative coagulation data should be evaluated; (2) sedative effects of benzodiazepines may be prolonged; and (3) serotonergic drugs such as meperidine, pentazocine, and dextromethorphan may predispose women to serotonin syndrome. SSRIs such as fluoxetine (Prozac) can antagonize the effects of the mu-opiate morphine, resulting in a decreased duration of analgesia; on the other hand, fluoxetine does not interfere with kappa-opiate drugs such as pentazocine. The popular sympathomimetic medication in obstetrics is ephedrine, and excitatory interaction has been reported after its use in patients taking fluoxetine. Because the SSRIs inhibit the cytochrome P450, amide local anesthetic metabolism may be inhibited; hence, precautions are necessary while using higher concentrations and volumes of local anesthetic in women taking SSRIs. Some of the SSRIs possess α_1 adrenergic antagonism. Exaggerated hypotension following spinal anesthesia has been reported following the use of risperidone.

Anti-fungal Drugs

Azole, antifungal drugs work by inhibition of a fungal cytochrome P450. Azoles are potent inhibitors of midazolam hydroxylation and thus can increase the concentration of midazolam.

Drugs Used During Labor and Delivery

Tocolytic Drugs

These drugs are commonly used for the treatment of preterm labor. They work by relaxing the uterus. Different groups of agents that have been used are (1) magnesium sulfate; (2) β-mimetic agents; (3) calcium channel blockers, e.g., nifedipine; (4) prostaglandin synthetase inhibitors, e.g., indomethacin; and oxytocin antagonists, e.g., atosiban.

Magnesium Sulfate

In many institutions in the United States, magnesium sulfate has become the tocolytic drug of choice. It might be the ideal agent for diabetic patients as well as for those with cardiac problems.

Magnesium sulfate can interact with both depolarizing and nondepolarizing muscle relaxants.[41–43] It can also reduce the minimum alveolar concentration of general anesthetics. Magnesium will cross the placenta freely and can cause neonatal hypotonia, hyporeflexia, and respiratory depression. Calcium can be used as a specific antagonist. Obstetric cases receiving magnesium sulfate may need less general anesthetic, and neuromuscular block should be monitored by a nerve stimulator if muscle relaxants are used.

β-*Mimetic Drugs*

Terbutaline and ritodrine are the most commonly used drugs in this class. Terbutaline is favored because it is less expensive, with similar incidences of side effects. It is important to take a note of the following drug interactions.

Central Nervous System. β-Mimetic drugs will stimulate the CNS and can cause agitation, restlessness, and tremors.

Cardiovascular System. Tachycardia, hypotension, and tachyarrhythmias are due to a direct effect of the drugs as well as an indirect effect from hypokalemia, which may be associated with the use of these drugs.

Respiratory System. Pulmonary edema is one of the complex problems associated with β-mimetic therapy. Its incidence has been noted to be as high as 5%.[44] The mechanism is not known, but three factors may be important: (1) left ventricular dysfunction, (2) low colloidal oncotic pressure,[45] and (3) increased pulmonary capillary permeability due to infection.[46] Volume expansion with large amounts of fluid can increase the incidence of pulmonary edema.

Metabolic Changes. Hyperglycemia, hyperinsulinemia, and consequent hypokalemia are possible side effects. Ketoacidosis can occur mainly in diabetic parturients.

Tachycardia can be worsened in the presence of other β-agonist drugs, such as epinephrine, ephedrine, and parasympatholytic drugs, such as atropine, and can increase the chance of tachyarrhythmias. Phenylephrine may be indicated to treat hypotension in such cases. Hypokalemia can also prolong the effect of nondepolarizing muscle relaxants.[47]

Calcium Channel Blockers

Nifedipine has been used successfully as a tocolytic drug. *Calcium channel blockers will potentiate the myocardial depressant effect of inhalational anesthetics.*[48] Uterine hemorrhage can be a potential problem. An important drug interaction between the Ca-channel blocker (nifedipine) and magnesium has been reported. Severe hypotension with cardiovascular collapse may occur.

Prostaglandin Inhibitors

Prostaglandin inhibitors like indomethacin can affect platelet function and can interfere with coagulation.

Oxytocin Antagonist

Atosiban is an oxytocin receptor antagonist. It has been used as a tocolytic agent to treat the initial episode of preterm labor as well as prolonging uterine quiescence by maintenance therapy.

Hypotensive Drugs

Hydralazine

Hydralazine will cause reflex tachycardia and can potentiate the effects of other drugs that are associated with maternal tachycardia.

Nitroglycerin

Nitroglycerin can be used for the treatment of hypertension or occasionally for uterine relaxation. It can affect the neuromuscular blockade produced by pancuronium.[49]

Nitroprusside

Consideration of cyanide toxicity in the mother should be addressed when nitroprusside is used for a long time in large doses. A systematic review of literature concluded that there is insufficient evidence for definitive conclusions about any direct association between sodium nitroprusside use and fetal demise.[50]

Trimethaphan

Trimethaphan, a ganglionic blocker, has been used to treat hypertension in preeclamptic cases. The drug interaction of trimethaphan and nondepolarizing muscle relaxants has been described.[51]

Uterotonic Agents

Different groups of agents are used to increase uterine contraction after delivery. Uterotonic agents include oxytocin, ergonovine maleate, methylergonovine maleate, and prostaglandins.

Oxytocin

Oxytocin is a commonly used agent for placental expulsion and the treatment of uterine atony. It is also used to induce or

augment labor.[52] Naturally occurring oxytocin is secreted by the posterior pituitary gland. Synthetic oxytocin is known as Pitocin or Syntocinon. Intravenous administration of Pitocin is associated with hypotension. Hypotension is well tolerated in healthy women because this effect is transient. However, it can be problematic in women with severe hypovolemia or under regional anesthesia.[53] The effect of intravenous oxytocin was studied during cesarean section under general anesthesia. A bolus of 10 units of oxytocin was associated with a decrease in femoral arterial pressure of 40%, systemic resistance of 59%, and pulmonary resistance of 44%, 30 s after injection. However, the heart rate increased 31% and stroke volume 17%, so that the cardiac output increased by 54%. The pulmonary arterial pressure and wedge pressure were increased by 33% and 35%, respectively, 150 s after injection. However, no changes were seen in the hemodynamic parameters during infusion of 80 mU/min oxytocin for 10 min.[54] Hence, it is suggested that this drug be administered via infusion rather than by bolus injection. It is prudent to restrain administering oxytocin as a bolus dose of more than 2 units. Our practice is to use infusions of oxytocin.

Synthetic oxytocin can cause antidiuretic responses in large doses.[55] Water intoxication, has been described following the infusion of larger doses of oxytocin. Use of isotonic saline solution in place of 5% glucose in water should diminish the risk of water intoxication.

Ergot Alkaloids

Ergonovine maleate (Ergotrate) and methylergonovine maleate (Methergine) are used for tetanic uterine contraction and are the drugs of choice when oxytocin fails to produce adequate uterine contraction. However, in contrast to synthetic oxytocin, these agents will cause maternal hypertension by causing direct peripheral vasoconstriction. Severe hypertension with cerebral hemorrhage has been described when intravenous methylergonovine is administered in combination with other vasoactive drugs such as ephedrine and phenylephrine.[56] Methylergonovine, 0.2 mg, should be administered

via intramuscular injection whenever indicated. It should not be administered in parturients with preeclampsia.

Prostaglandins

$PGF_{2\alpha}$ is the drug of choice if uterine contraction is not effective following the use of oxytocin and methylergonovine. *Transient hypertension, severe bronchoconstriction, and pulmonary vasoconstriction have been described following the use of* $PCF_{2\alpha}$.[57] Careful attention is needed while using $PCF_{2\alpha}$ in patients receiving vasopressors or agents that cause bronchoconstriction (propranolol). Carboprost (Hemabate, a 15-methyl analog of naturally occurring prostaglandin F2α) is administered (0.25 mg) via intramuscular route or can be injected directly into the myometrium by the obstetrician.

Local Anesthetics

Of the two groups of local anesthetics (ester vs. amide) *ester local anesthetics are mainly associated with allergic reactions because of the metabolic product para-aminobenzoic acid.*

Chloroprocaine is the ideal local anesthetic to use in the presence of fetal distress and acidosis. *Mean in vitro half-lives of 11 ± 2.8 s and 15.4 ± 5.2 s have been described for maternal and fetal plasma, respectively, whereas the in vivo half-life was found to be 3.1 ± 1.6 min* in maternal plasma.[58] Only one case of maternal grand mal seizures has been reported; this was associated with abnormal cholinesterase activity. In this case, the dibucaine number was zero.[59]

Interesting drug interactions have been described between chloroprocaine and bupivacaine's effectiveness. The effective duration of bupivacaine has been observed to be shortened when it is used after chloroprocaine.[60] The mechanism is not known. The effects of μ-receptor agonist drugs such as fentanyl and morphine have also been observed to be shortened following the use of chloroprocaine.[61] Chloroprocaine or its metabolites may act as a μ-receptor antagonist. However, this mechanism of μ-receptor antagonist has not been substantiated.[62]

The use of bicarbonate in combination with a local anesthetic has become popular because of faster onset. Several mechanisms have been suggested. Increased pH, with a more basic form of the local anesthetic, and the effect of CO_2 have been proposed.[63] Using 8.4% of bicarbonate, the solution should be 1 ml in 10 ml for lidocaine, 1 ml in 10 ml for 2-chloroprocaine, and 0.1 ml in 20 ml for bupivacaine. There is possibility of precipitation, especially with bupivacaine.

Narcotics

The *use of agonist–antagonist medication either parenterally or epidurally in women addicted to narcotics can trigger an acute abstinence syndrome* characterized by tachycardia, tachypnea, diaphoresis, hypotension, abdominal cramps, and agitation and apprehension.[64]

Drugs Used for Fetal Indications

At present, different agents are used maternally to treat fetal arrhythmias. These abnormal rhythms in the fetus are usually due to defects in the conduction system that are either anatomic or related to viral infection. Digoxin, verapamil, quinidine, procainamide, and propranolol have been used in mothers in the hope that these drugs will ultimately reach the fetus via the placenta. Important drug interactions may occur between these drugs and other agents that may be used for maternal indications. *Maternal plasma levels should be monitored for therapeutic digoxin levels. The plasma potassium concentration is also important because low plasma potassium levels exacerbate digoxin toxicity. Mothers receiving β-blockers may need higher doses of ephedrine to treat hypotension following regional anesthesia. On the other hand, ephedrine might be detrimental in the presence of fetal tachyarrhythmias; smaller doses of phenylephrine may be indicated* in such a situation. However, if there is associated congenital fetal bradycardia, phenylephrine use is controversial.

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5
Uteroplacental Blood Flow

Maintenance of uteroplacental blood flow is essential for fetal well-being; hence an in-depth knowledge of this subject is essential for individuals taking care of pregnant women.

Uterine blood flow is determined by the equation

$$\frac{\text{Uterine arterial pressure} - \text{uterine venous pressure}}{\text{Uterine vascular resistance}}$$

Hence any condition that will *significantly decrease mean maternal arterial pressure or significantly increase uterine vascular resistance* will decrease uteroplacental blood flow. Placental blood flow and, ultimately, umbilical blood flow, is the key determinant of fetal well-being. The normal placental vasculature is vasodilated (though not, as is commonly misunderstood, maximally so). Nitric oxide production in the uterine

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circulation of pregnant but not nonpregnant animals appears responsible for much of the vasodilation in normal pregnancy. Thus placental blood flow will mainly depend upon upstream blood pressure in the uterine circulation.

Measurement of Uteroplacental Blood Flow

Because of the absence of practical noninvasive techniques, most of the data regarding uteroplacental blood flow comes from animal experiments. Formerly, radioactive xenon (^{133}Xe) was used to measure uterine blood flow in humans, but this technique has fallen out of favor due to the exposure of the fetus to radioactivity. Over the last two decades, Doppler ultrasound measurement of uterine and umbilical arterial velocity waveforms has been used with some success.[1] The ratio of the peak systolic velocity and diastolic trough of blood flow velocity (*S/D*) has been observed in different clinical settings, and a *high S/D ratio is associated with reduced placental perfusion* (Fig. 5-1). Absent or reversed diastolic flow in the umbilical artery is also associated with poor outcome in hypertensive disease of pregnancy and intrauterine growth restriction (IUGR). In addition, pulsatile flow in the umbilical vein is associated with poor prognosis in cases of IUGR and is considered an indication for delivery.

Clinical Implications of the Uteroplacental Circulation: Gas Exchange Across the Placenta

The uteroplacental circulation is directly involved with respiratory gas exchange in the fetus, and it is useful to think of the placenta as fulfilling the role played by the lung in the postnatal period. Fetal oxygenation depends on the uterine artery oxygen content and umbilical vessel blood flow. Fetal oxygen transfer also depends on oxygen affinity and the oxygen-carrying capacity of maternal and fetal blood. The oxygen-carrying

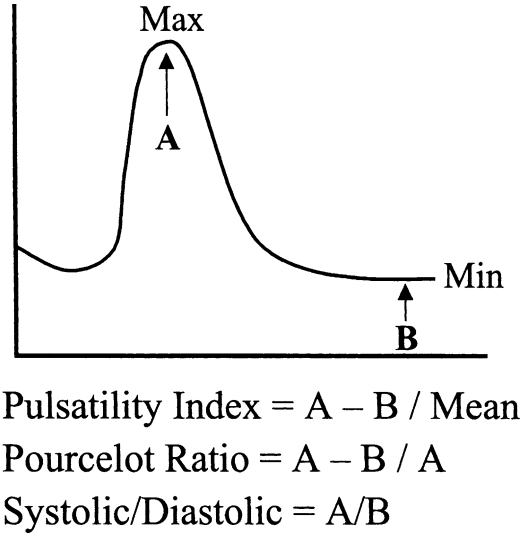

Figure 5-1. Umbilical blood flow velocity.

capacity will ultimately depend on hemoglobin concentration and the oxyhemoglobin dissociation curve (oxygen affinity). The oxygen dissociation curve is shifted to the left in the fetus as compared with the mother due to the greater affinity of fetal hemoglobin for oxygen when compared to the adult form. The hemoglobin concentration of fetal blood is high (16–18 g/100 mL) when compared with the mother (12 g/100 mL). Hence, the higher oxygen affinity as well as the higher oxygen-carrying capacity of fetal blood benefits the fetus by increasing oxygen uptake across the placenta. Together, these mechanisms assure that oxygen content in the fetal blood approaches that of the adult, despite the low PO_2 (approximately 30 mmHg) in the umbilical vein, the major vessel providing oxygen to the fetus.

Healthy fetuses can tolerate a decrease of 40–50% oxygen delivery without any untoward effect, because of fetal reserve and various compensatory mechanisms.[2] Animal studies have shown that fetal oxygen delivery averages 24 mL O_2/min/kg and that oxygen consumption is 3 mL O_2/min/kg.

Compensation takes place either by increased oxygen extraction or by redistribution of the fetal circulation. Under hypoxic conditions, the fetus redistributes blood flow preferentially to vital organs, including the brain, heart, and adrenal glands.[3] Circulating vasopressin may play a role in this redistribution of the fetal circulation.[4]

Carbon dioxide (CO_2) exchange also depends upon umbilical as well as uterine blood flow. Acute respiratory acidosis can be caused by an accumulation of CO_2 because of a decrease in either uterine or umbilical blood flow. Maternal hypocapnia, conversely, may be associated with fetal hypoxia and acidosis. Three mechanisms have been suggested for this (Fig. 5-2): (1) maternal hypocapnia (<25 mmHg) causes uterine and umbilical vessel vasoconstriction; (2) mechanical hyperventilation increases intrathoracic pressure and reduces venous return as well as cardiac output and thus reduces uteroplacental blood flow[6]; and (3) maternal alkalosis shifts the oxygen–hemoglobin dissociation curve to the left, reducing fetal extraction of oxygen.[5]

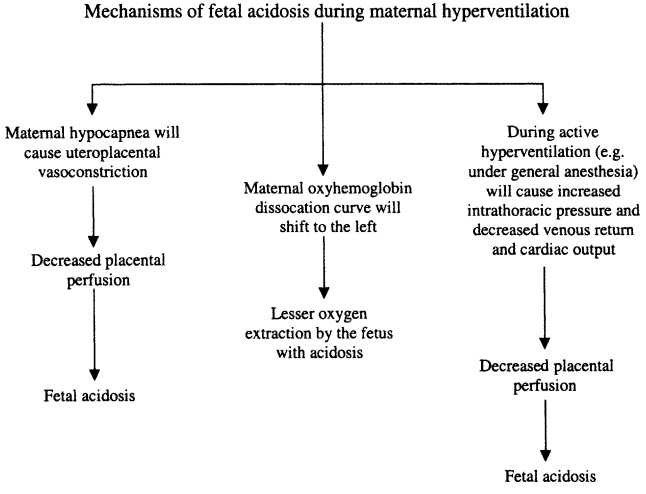

Figure 5-2. Mechanisms of fetal acidosis during maternal hyperventilation.

Factors That Can Alter Uteroplacental Blood Flow

Because the uteroplacental circulation is generally vasodilated, the most important determinant of uteroplacental blood flow (UBF) is maternal blood pressure in the uterine artery. Decreased mean maternal artery pressure will reduce uterine artery blood flow and ultimately uteroplacental blood flow. *Aortocaval compression by the large gravid uterus (supine position) is one of the main causes of decreased uterine blood flow*. Besides this important mechanism, other factors that can potentially decrease uterine blood flow are (1) sympathectomy from regional anesthesia (see below) and (2) hypovolemia from severe hemorrhage. A number of other factors can also alter UBF.

Uterine Contraction

Uterine contraction reduces uteroplacental blood flow. Measurement of intrauterine pressure (IUP) in labor demonstrates that uterine artery blood flow during diastole decreases during contractions as pressure rises and falls to zero when IUP reaches 35–60 mmHg.[6] Fetal umbilical blood flow is much less affected, however, and the fetus can generally compensate for the short-lived interruption of circulation. However, if fetal reserve is already compromised or if there is tetanic contraction, fetal asphyxia can occur.

Pain and Stress of Labor

Labor pain causes significant increases in sympathetic nervous system activity and circulating maternal catecholamines.[7] In animal models, stress of this magnitude causes a sharp decrease in uterine blood flow.[8] In addition, unmedicated parturients may hyperventilate, which can reduce uterine blood flow further.[9]

Regional Anesthesia

The effect of epidural or spinal anesthesia on uterine blood flow is complex and difficult to predict in a given patient.

In the absence of hypotension, several studies in both gravid sheep models as well as humans show no change in uterine blood flow.[10,11] Conversely, relief of pain may decrease sympathetic activity and hyperventilation, increasing uterine blood flow, particularly in preeclampsia.[12] Hypotension from regional anesthesia, however, can decrease uterine blood flow, and unintentional intravenous local anesthetic injection can result in both uterine hypertonus and maternal hypotension, both of which would reduce uterine blood flow. Finally, the rapid pain relief following combined spinal-epidural analgesia has been associated with fetal bradycardia, which may reflect transient decrease in uterine blood flow due to changes in circulating maternal catecholamines.[13]

Pathological Conditions

Any condition that increases vascular resistance across the intervillous space will result in reduced uteroplacental blood flow at a given maternal blood pressure. The three most important maternal pathological states that reduce placental perfusion are (1) pregnancy-induced hypertension and preeclampsia, (2) diabetes, and (3) postdates or postmature pregnancy (>42 weeks' gestation).

Pharmacological Agents

Intravenous Induction Agents

Any induction agent that lowers maternal blood pressure can transiently reduce uteroplacental blood flow. However, these drugs are usually administered just prior to laryngoscopy and endotracheal intubation, which causes an increase in sympathetic activity and circulating catecholamines, which can reduce uterine blood flow further.[14]

Barbiturates. In sheep studies, thiopental given for induction and intubation decreased uteroplacental blood flow, presumably by reducing maternal blood pressure but also likely due to stress-induced uterine constriction.[15] Other studies have documented uterine artery constriction following induction with thiopental.[16]

Propofol. Propofol is associated with a greater decrease in blood pressure than thiopental when used for induction of anesthesia.[17] This would logically be associated with a greater decrease in uteroplacental blood flow. However, pregnant sheep given propofol showed no change in blood flow during induction or intubation.[15]

Ketamine. Ketamine has been studied in sheep at doses between 0.5 mg/kg and 0.7 mg/kg.[18] Maternal blood pressure and cardiac output increased, as did resting uterine tone, but uterine blood flow did not change. In humans, doses up to 1.1 mg/kg caused only mild (<10%) increases in uterine tone[19] and did not affect the clinical or the acid–base status of neonates following either vaginal delivery or cesarean section.[20] Ketamine is rarely used electively, but in the setting of hemorrhage or other causes of hypovolemia, its ability to maintain maternal hemodynamic stability may be beneficial.

Other Agents. Etomidate is another cardiovascularly stable induction agent which has been occasionally used in obstetrics, particularly in the setting of severe maternal cardiac disease. In the pregnant ewe, fetal effects are minimal.[21] In humans randomized to etomidate or methohexital for induction prior to cesarean section, no adverse effects of etomidate were noted other than transient reduction in neonatal cortisol.[22] Benzodiazepines are uncommonly used for induction of anesthesia in present practice. Older studies found no effect on uteroplacental blood flow in relatively large doses of diazepam, unless maternal hypotension occurred.[23] Midazolam caused even fewer effects.[24] It is likely that small doses used for intravenous sedation during regional anesthesia would have a negligible impact.

Inhalation Agents

All inhalation anesthetics cause dose-related decreases in maternal blood pressure, though the hemodynamic mechanism responsible varies somewhat, with halothane producing less vasodilation than isoflurane, sevoflurane, and desflurane. When used in clinically relevant concentrations of 0.5–1.5 minimum alveolar concentration (MAC), all have proven satisfactory for cesarean delivery. Animal experiments with such

doses of isoflurane and halothane show that uteroplacental blood flow is preserved despite modest reduction in maternal blood pressure, likely due to uterine artery vasodilation below resting (pre-induction) tone.[25] However, larger doses of halothane (1.5%) caused decreased uterine blood flow in monkeys, likely because the decrease in maternal blood pressure overwhelmed any compensatory vasodilation in the uterine circulation.[26] Newer low-solubility agents (sevoflurane, desflurane) have been successfully employed in cesarean delivery and allow more rapid titration of concentration after delivery (to avoid excessive uterine relaxation) and emergence after anesthesia.[27,28]

Local Anesthetics

In addition to the hemodynamic effects of local anesthetics used for regional anesthesia discussed earlier, these drugs may have direct effects on uterine blood flow. In vitro studies on human uterine arteries obtained from pregnant and nonpregnant uteri showed that high doses of the local anesthetics lidocaine and mepivacaine (400–1,000 μg/mL) caused uterine artery vasoconstriction only in specimens obtained from pregnant uteri.[29] This observation is likely related to the ability of local anesthetics to block endothelium-dependent relaxation by nitric oxide,[30] which is increased in the pregnant state.

The vasoconstrictive effects observed in these studies were seen with concentrations that could only be achieved in a clinical situation by injecting local anesthetics intravenously while performing epidural anesthesia or perhaps during performance of a paracervical block (an outdated technique which is associated with fetal bradycardia, most likely due to uterine artery vasoconstriction).[31]

Lower concentrations of lidocaine (blood level, 2–4 μg/mL), similar to those produced during properly performed epidural anesthesia, do not decrease uterine blood flow even after prolonged infusion.[32] Ropivacaine and bupivacaine also do not cause vasoconstriction or reduce uteroplacental blood flow in concentrations produced during regional anesthesia.[33] On the other hand, cocaine is associated with dose-related uterine

vasoconstriction and reduction in uterine blood flow[34] and this effect does occur at clinically encountered concentrations.[35]

Epinephrine

Epinephrine is frequently added to local anesthetics to intensify the sensory and motor blockade as well as prolong the duration of anesthesia. Epinephrine possesses both α- and β-adrenergic effects. Fifteen micrograms of epinephrine has been suggested as an intravascular test dose. Doses of this magnitude produce dose-dependent but short-lived decreases in uterine blood flow in pregnant sheep.[36] Systemic absorption of epinephrine from the epidural space produces effects similar to intravenous injection of very low doses. Beta effects predominate (increased heart rate and cardiac output, decreased vascular resistance and arterial pressure) and uteroplacental blood flow may decrease.[37]

Opioids

Fentanyl is commonly added to local anesthetics used in epidural analgesia. In pregnant ewes, it has no effect on uterine blood flow.[38] Intrathecal opioids, especially meperidine, which has a local anesthetic-like effect, but also sufentanil, because of pain relief and possibly sympathetic blockade, can lower maternal blood pressure and thus potentially reduce uterine blood flow.

Vasopressors

Ephedrine, which has mainly a β-adrenergic effect, has for several decades been considered the drug of choice for the treatment of hypotension in the parturient. Ephedrine increases the blood pressure by both ionotropic and chronotropic effect on the heart as well as increasing venous return (preload).[39] In addition, ephedrine causes release of nitric oxide in the pregnant uterine circulation, helping to preserve uterine blood flow.[40] Classic experiments suggested, conversely, that vasopressors which have mainly α-adrenergic effects (mephentermine, metaraminol, methoxamine) increase the blood pressure

primarily by peripheral vasoconstriction, with a significant reduction in uterine blood flow.[41] In the past two decades, however, numerous comparative trials have failed to confirm this advantage in the clinical setting. The difference may be due to the very large doses of alpha agonists used in classic sheep studies, or perhaps to a species difference. The results from seven RCTs in human clinical use show no difference in efficacy or neonatal outcome (clinical acidosis, Apgar scores), but a small benefit in neonatal pH (mean 0.03 units) favoring phenylephrine.[42] Two cautions should be noted when interpreting this finding, however: (1) widely different assumptions on relative potency of the drugs have been employed, sometimes leading to very high doses of ephedrine being administered; and (2) only healthy parturients undergoing elective cesarean delivery were studied. Indeed, in a compromised fetal sheep model, phenylephrine used to correct epidural-induced hypotension caused marked fetal deterioration when compared to ephedrine.[43] We therefore recommend either drug for use in elective surgery, but consideration for ephedrine as a first choice when impaired uteroplacental circulation is suspected on the basis of maternal history or the fetal heart rate tracing.

Antihypertensive Agents

Hydralazine. Hydralazine is a direct smooth muscle dilator and is a commonly used hypotensive agent in preeclampsia. In animal studies, hydralazine decreased maternal blood pressure and improved uteroplacental blood flow better than nitroglycerin.[44] In parturients with preeclampsia, however, hydralazine decreased maternal blood pressure but did not improve blood flow as estimated by Doppler ultrasound of uterine arterial branches.[45]

Nitroglycerin and Nitroprusside. These drugs reduce blood pressure by producing nitric oxide. In pregnant sheep, nitroglycerin administered after phenylephrine-induced hypertension decreased maternal arterial blood pressure and caused an increase in uteroplacental blood flow.[46] Nitroprusside is also effective at restoring uteroplacental blood flow in norepinephrine-induced hypertension in sheep.[47]

Unfortunately, there is no direct evidence regarding the effectiveness of either agent in humans, nor in the clinical situations in which they would be considered (e.g., severe preeclampsia).

Calcium Channel Blockers. In animals, verapamil decreases maternal arterial pressure and reduces uteroplacental blood flow.[48] Nifedipine is now considered the drug of choice for short-term tocolysis in preterm labor by many authorities. This drug has been studied in humans with Doppler estimation of effects on uteroplacental blood flow and no significant changes were noted following nifedipine loading of up to 40 mg.[49]

β–Adrenergic Blocking Drugs. Maternally administered esmolol produces β-adrenergic blockade and hypoxemia in fetal sheep, although the effect on uteroplacental blood flow was not measured.[50] Esmolol likely undergoes rapid placental transfer, and thus may directly slow the fetal heart rate. Bradycardia requiring emergency cesarean delivery has been reported in humans.[51] Labetolol is an increasingly popular drug for blood pressure control in preeclampsia. It has mixed beta- and alpha-adrenergic blocking effects and does not reduce uterine blood flow in humans.[52]

Tocolytic Drugs (Magnesium Sulfate, Beta Adrenergic Agonists, Indomethacin)

Tocolysis is commonly performed in modern practice only for short periods (<48 h). Magnesium causes mild uterine artery dilation in animals and humans with preterm labor and preserves uteroplacental blood flow during epidural anesthesia-induced hypotension.[53] Other drugs used for tocolysis do not have important effects on uteroplacental blood flow.

Summary

Different anesthetic techniques and agents will affect uteroplacental blood flow and ultimately fetal well-being. Hence, appropriate knowledge of uteroplacental physiology and pathology is important for the obstetric anesthesiologist.

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6
Pain of Labor and Delivery

Labor and delivery are complex processes resulting in the expulsion of the fetus and placenta from the mother. The cause of the onset of labor is unknown. Factors such as increased prostaglandin production, an increase in oxytocin receptors, and increased myometrial gap junction formation have been postulated as the causes of onset of labor.[1,2] The labor and delivery process has been divided into three specific stages.

1. *The first stage starts from the start of regular uterine contractions (progressive cervical dilatation associated with regular uterine contraction) until the completion of cervical dilatation. It is commonly divided into a latent phase and an active phase, the latter being characterized by a rapid acceleration of cervical dilatation.*
2. *The second stage starts from full dilatation of the cervix until the delivery of the infant.*
3. *The third stage starts from delivery of the infant until the time of expulsion of the placenta.*

The distinction of labor into various stages is important to anesthesiologists because the pain impulses follow different pathways during each stage of labor. Labor pain has a visceral component and a somatic component. Uterine contractions may result in myometrial ischemia resulting in the release of potassium, bradykinin, histamine, and serotonin, In addition, mechanoreceptors are also stimulated by the stretching and distention of the lower segments of the uterus and the cervix.[3] Pain during the first stage of labor is mediated through the afferent nerves supply of the uterus via sympathetic nerve, which ultimately reach the T10–L1 segments of the spinal cord. The first stage of labor pain has been described as referred pain to the back and anterior abdominal wall. This is because the lower back and anterior abdominal wall are innervated by the same spinal segments that receive pain impulses from the uterus

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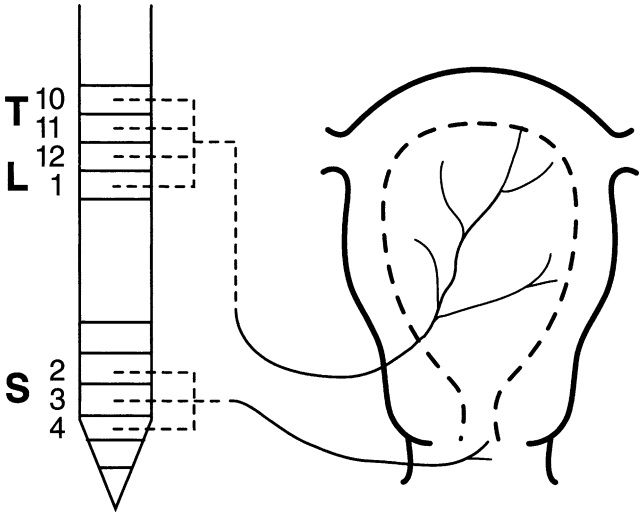

Figure 6–1. Pain pathways for the first and second stages of labor.

(Fig. 6-1). The nerves from the uterus together with other autonomic nerve fibers from the cervix form the inferior hypogastric plexus; fibers from this plexus traverse along the iliac vessels as the right and left hypogastric nerves. These nerves ultimately communicate with the superior hypogastric nerve and reach the sympathetic chain either directly or via the aortic plexus. These finally reach the spinal cord via the posterior nerve root ganglion. Some of the nerve fibers from the ovary, uterine ligaments, and fallopian tubes travel via ovarian nerves and ultimately reach the spinal cord via the aortic plexus and sympathetic chain. The nerves in the spinal cord relay to neurons of the posterior horn cells and ultimately reach the central nervous system via the lateral spinothalamic tract.

Pain during the second stage of labor follows a different pathway from the first stage of labor. Pain for the second stage of labor is carried by the pudendal nerve (S2, S3, S4). This nerve originates from the sacral plexus and accompanies the pudendal vessels and crosses the ischial spine to innervate the

perineum and the vagina. The nerve is easily accessible for local anesthetic block at the level of ischial spine.

Pain Score of Labor Pain

The McGill pain questionnaire ranks labor pain in the upper part of the pain scale between that of cancer pain and amputation of a digit (Fig. 6-2).[4] The American College of Obstetricians and Gynecologists, in their committee opinion #118, summarize pain relief during childbirth as follows: "Labor results in severe pain for many women. There is no other circumstance where it is considered acceptable for a person to experience severe pain, amenable to safe intervention, while under a

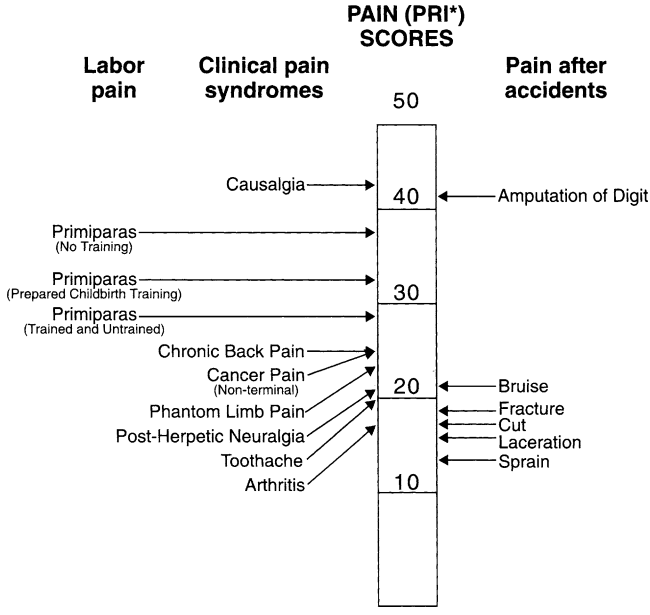

Figure 6–2. Comparison of pain scores by using the McGill pain questionnaire. (Adapted from Melzack.[4])

physician's care. Maternal request is a sufficient justification for pain relief during labor." [5]

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7
Non-pharmacological Methods for Relief of Labor Pain

Although systemic medications and regional anesthetics have become popular in recent years, other techniques that do not involve medication have also been tried in different centers with varying success. There are instances where a mother may not wish to use medications or regional analgesia for childbirth, or pharmacological options may not be available in some parts of the world. In these situations the non-pharmacological methods have been found by many laboring mothers to assist in dealing with the pain of labor. These techniques include hypnosis, psychoanalgesia (natural childbirth and psychoprophylaxis), the Leboyer technique, acupuncture, transcutaneous electrical nerve stimulation (TENS), aromatherapy, touch and massage, maternal movement and positional changes during labor, and water birthing.

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Hypnosis

Hypnosis has been used for relief of labor pain for a long time. Hypnobirthing was introduced in the nineteenth century utilizing techniques for fear release and relaxation. "Women attempt to relieve all anxiety and reach a loose, limp, rag-doll relaxed state, then the body can do what it was designed to do during birth, without limitation and resulting discomfort."[1,2] Hypnobirthing classes often meet once a week for 2 h a class beginning at the 30th week of pregnancy over a 4- to 5-week period. The hypnotherapist usually does not accompany the mother in the birth. This method attempts to modify the perception of pain through self-hypnosis and post-hypnotic suggestion. An example is the imagining of being in a safe place often symbolizing the pain as something that can be separated from conscious recognition thereby attempting to recognize less pain. Some goals of hypnotherapy include: reduced need for pain medications, less fatigue from labor, bringing together mother and the baby, and decreasing hyperventilation. This method also attempts to make the birthing process less scientific through the replacement of conventional birthing terminology with less scientific descriptives. Examples of this include calling the birthing coach a birthing companion, catching the baby is called receiving the baby, and uterine contraction is referred to as uterine surge.

Hypnotherapy has no recognized risk factors to the mother or the unborn fetus. Some of the recognized disadvantages include[1–3]: one randomized trial has shown the mean duration of labor to be longer in the hypnosis group; decreased popularity among many obstetricians because of the increased time required for adequate hypnosis preparation compared to standard medical pain relief methods; the level of hypnotic state required to tolerate pain of birthing may lessen the memory of the birth process; and relatively small success rate of adequate hypnosis. The advantages of this technique include minimal maternal and fetal physiological interference.[1–3]

Psychoanalgesia

Natural Childbirth

Dick-Read originated this concept in the 1940s.[4] He explained the mechanism of labor pain in relation to anxiety and fear and prepared women to have a determined fearless approach to labor in order to minimize pain. Dick-Read is probably is the first to advocate using controlled breathing and relaxation techniques during labor. A major study at Yale New Haven Hospital in 1946 showed that using techniques based on the Dick-Read method decreased the amount of anesthesia during labor. Presently, there are several nursing groups who encourage pregnant women to learn the breathing techniques during antenatal preparatory sessions. Women are encouraged to pursue these techniques before opting for pharmacological methods of pain relief. However, the final success is variable as this method requires substantial motivation from all participating members for the entire duration of pregnancy, labor, and delivery.

Psychoprophylaxis

Lamaze is the originator of this psychoanalgesic technique, and it became very popular among women who tried to avoid medications during labor and delivery. This technique involves education of parturients regarding "positive" conditioned reflexes. It involves continuous labor support (by the monitrice or doula) and the use of a repertoire of relaxation and breathing strategies. Lamaze believed that controlled, conditioned breathing exercises were effective in blocking women's perception of pain of contractions. The advantages of this procedure include the avoidance of any medications which disturb maternal physiology, as well as avoidance of fetal depression from narcotics. However, the success rate of this technique varies considerably, and parturients may request systemic medications or regional analgesia when using this technique. Interestingly, one study shows that parturients prepared for delivery using psychoprophylaxis techniques need

less analgesia during labor and delivery than unprepared parturients.[5]

Leboyer Technique

In 1975 the French obstetrician Leboyer described "birth without violence."[6] According to the author the psychological birth trauma of the neonate can be reduced by avoiding noise, bright lights, and other stimulating events of the delivery room. Hence Dr. Leboyer believed in delivering the baby in a silent semi-dark room and also avoiding stimulation of the newborn immediately after the delivery. Earlier, in Boston Hospital for Women, Leboyer delivery was popular among a few obstetricians in conjunction with either systemic medication, local anesthetic via the epidural route, or no medication. Anesthesiologists and neonatologists faced unique issues such as problems with maintenance of neonatal temperature and improper lighting for adequate evaluation of the babies.

Acupuncture

Acupuncture techniques have been used in China both for surgery as well as for pain relief. It has been used for thousands of years to assist with pain control, addiction, nausea/vomiting, and many other purported uses. In theory there are more than 365 points along the 12 meridians (energy paths) of the body. Interruptions of energy flow (surgery, labor etc.) along meridians break up the harmony of the body producing feelings of pain or uneasiness. Very fine needles are placed at specific points to redirect energy to correct paths that has been interrupted by surgery or labor. It is hypothesized that acupuncture works by interrupting or inhibiting pain impulses sent to the brain or the stimulation of endorphins in the body. Very fine sterile needles are placed just under the skin at strategic points along the body by a trained acupuncture professional. These needles are left in place for varied amounts of time and are often connected to a small electrical current to assist in pain control. Acupuncture may be done for several weeks prior to

delivery in weekly hour-long sessions. Limitations include: needles need to be placed by an acupuncture professional, risk of infection at needle site, and placement of needles in labor may limit the mobility of the mother.

While most studies have shown no difference in the production of endorphins some suggest there is a shortened first stage of labor when acupuncture is administered over multiple sessions several weeks before birth. However, the reported shorter first stage of labor could be inaccurate as these studies were not consistent in measuring the duration of first stage of labor. In a recent Swedish study, acupuncture was administered by midwives who had gone through a 4-day course on the use of acupuncture during labor. This study found that "women who received acupuncture were half as likely to request an epidural during labor, and less likely to ask for other types of pain relief, such as nerve stimulation therapy or a warm rice bag." However, the treatment appeared to have no significant effect on how much pain the women said they were feeling, according to the report in the *British Journal of Obstetrics and Gynaecology*.[7] Recently, there has been a considerable interest in this technique where the authors noted acupuncture could reduce pain experience, active phase duration, and oxytocin units. Patients were satisfied with the technique and no adverse effects were noted.[8] However, another study did not replicate these results.[9] Acupuncture might be more effective for nausea and vomiting of labor than labor pain relief.[10]

Transcutaneous Electrical Nerve Stimulation (TENS)

TENS has been used for chronic pain therapy as well as relief of acute postoperative pain. Although the mechanism is not exactly known, the different hypotheses that have been put forward are (1) modulation of the pain impulse reaching the substantia gelatinosa and (2) liberation of endogenous opioids.[11,12]

TENS has been used for the relief of labor pain with variable success. Skin electrodes of conductive adhesive are placed over the T10–L1 spinal region bilaterally; TENS can also be applied

in the sacral area during the second stage of labor. Because of its inconsistent success, this technique has never become popular in this country.[13]

Aromatherapy

Aromatherapy has garnered attention recently as a way to promote stress relief during labor. More and more women are turning to aromatherapy during their labor to help them cope with the emotional issues facing them. There is no direct or indirect pain relief involved but the laboring mother may find aromatherapy helps reduce stress thereby allowing pain to be better tolerated. Some suggest aromatherapy also promotes stress reduction among helping caregivers and loved ones making the overall environment better. Essential oils of rose, lavender, neroli, clary sage, and others are placed in baths, on face cloths, in massage oil, or directly on the laboring mother's skin. Many recommend picking a few different oils to use at different stages of labor. Suggestions include the use of calming oil for the first stage of labor before the baby begins to descend. As stage 2 of labor begins with the descent and delivery of the baby, oil like peppermint has been found by many to promote a sense of strength. Limitations include absence of direct effect on pain relief, some women may have allergic reactions to particular oil preparations, and many laboring women are particularly sensitive to certain smells that may enhance nausea and vomiting associated with labor. While there are no good studies demonstrating benefit to the laboring mother, the minimal risks and costs associated with aromatherapy make this a good adjunct in many laboring women. It may be wise for the mother to pick out pleasing oil blends prior to the onset of labor. This can help prevent using scents that enhance nausea and vomiting.

Touch and Massage

Many mothers appreciate touch and massage while in labor. Most often the provider of this is a loved one or supporter. While there is a lack of quality studies of the benefit of touch

and massage it is clear that mothers receive significant emotional and physical relief. Therapeutic touch and massage can include a wide variety of hands-on interventions for the mother ranging from therapeutic massage to light caressing and hair stroking. This may include the use of hands, fingertips, or devices to stroke and apply pressure relieving pain and facilitating relaxation. Mothers may be better able to tolerate the pain of labor with better relaxation and a lower baseline level of anxiety.

Many women feel lower back pain associated with the posterior position of the baby's head. Massage of pressure on this area can provide relief from this pain. Pain relief may occur through stress reduction, distraction, or through the stimulation of other receptors. The benefit of pain relief from this modality has not been shown to decrease the utilization of pain medications or other medical interventions. The pain relief in birth appears to last approximately 30 min when massage or deep pressure is used. Therefore, massage may work best when given in 30-min intervals with breaks in between.[1,14]

Maternal Movements and Positional Changes

Laboring women find some positions and movements more comfortable than others in different stages of labor. Since the early 1900s birthing has moved from the home to the hospital with the use of medical staff, intravenous lines, epidurals, and other forms of medical care. This may have served to limit the freedom of movement of the birthing mother. When the mother alters position, she changes the relationships between various factors such as baby's head position, pelvis, and gravity. Movements and positioning changes in labor may be recommended to rotate a malpositioned baby and enhance progress of labor in dilation and baby descent. Many studies suggest walking or sitting more upright speeds the rate of labor. Some sample positions include upright, squatting, side, flat, and hand and knees position. Recently birthing balls have been used to provide comfort during labor. The mother can sit, rock, bounce, or stretch on the inflatable ball to ease pain or increase the rate of delivery. No studies have reported any position that has been

found to be harmful to the baby or mother. Women should be encouraged to seek any position that provides comfort and maintain an upright position if she wishes. Certain procedures such as epidurals may make ambulation unsafe even with adequate leg strength. Many labor units lack manpower or designated areas to facilitate walking with epidural placement. Birthing balls should not be used without the assistance of experienced caregivers to prevent against falls.[1,2,14]

Water Birthing

Another natural childbirth option that has become popular is water birth. Water birth provides a calm, relaxing atmosphere for both the expectant mother and her newborn.

Summary

Ultimate success from the techniques described above predominantly depends upon the parturient's own motivation; hence the success of these methods varies widely, and thus these modes have never been universally accepted.

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8
Relief of Labor Pain by Systemic Medications and Inhalational Agents

Systemic medications have been used exclusively or in association with psychoanalgesia for relief of labor pain during both the first and second stages of labor. These drugs can be classified into several categories.

Opioids

Opioids are popular agents for the relief of labor pain either in an early stage before the administration of epidural analgesia or throughout the first and second stages of labor. Because of their faster action and more reliable plasma concentrations, most of these agents are used intravenously. The various narcotics that can be used are as follows:

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Morphine

One of the most effective pain relievers, morphine, used to be a popular agent; however, because of the *possibility of a higher incidence of neonatal respiratory depression* this agent is not popular for obstetric patients at the present time. It is used either intramuscularly (5–10 mg) or intravenously (2–3 mg), and its peak effect occurs at 1–2 h and 20 min, respectively.[1] Ten healthy nulliparous parturients in active labor were given doses (up to 0.15 mg/kg body weight morphine) for pain relief. The parturients were all significantly sedated and several fell asleep but were awakened by pain during contractions.[2]

Meperidine

This is the most commonly used drug at the present time because of its fast onset. It is used both intramuscularly (50–100 mg) and intravenously (25–50 mg), and its time of onset is 40–50 min and 5–10 min, respectively. Meperidine rapidly crosses the placenta and attains fetal and maternal equilibrium within 6 min.[3]

An interesting observation associated with maternally administered meperidine was the higher incidence of neonatal respiratory depression when the delivery took place during the second and third hour of drug administration. No significant respiratory depression of neonates was observed when delivery took place within 1 h or 4 h after drug administration.[4] Kunhert et al. did an extensive study to explain this interesting observation; these authors measured umbilical cord and neonatal urine concentrations of meperidine and normeperidine and found that neonatal urine meperidine concentrations showed the highest amount of drug transfer to fetal tissues after 2–3 h of maternal administration (Fig. 8-1).[5] Normeperidine, a metabolite of meperidine, reached its highest fetal concentration after 4 h of maternal administration (Fig. 8-2). They also observed poor Brazelton neonatal neurobehavioral scores at both 12 h and 3 days of age; according to these authors this is related to normeperidine. Thus, the immediate fetal effect observed after the maternal administration of meperidine as shown by low Apgar scores most probably is related to the direct effect

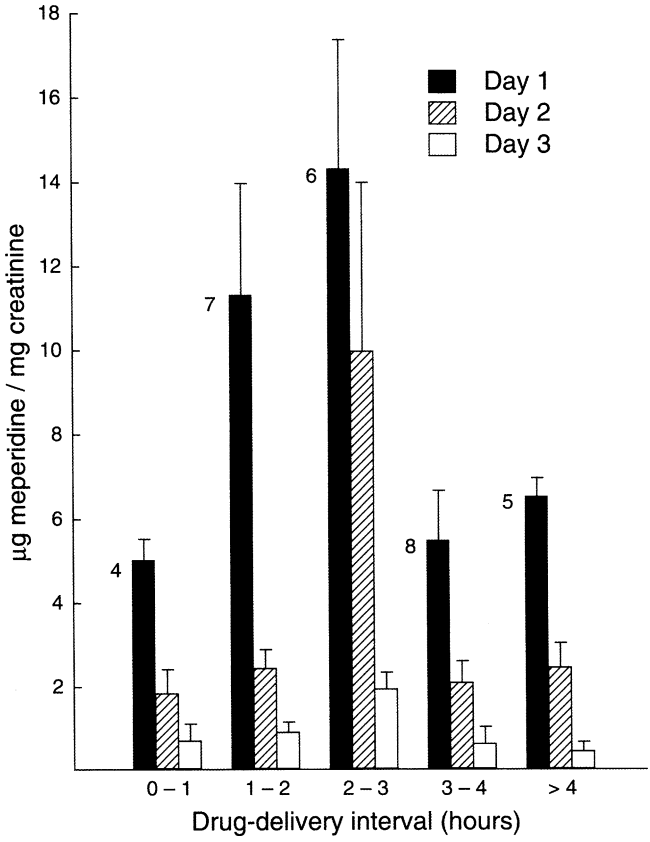

Figure 8–1. Relationship between the meperidine delivery interval and urinary excretion of meperidine by the neonate. (Adapted from Kuhnert et al.[5])

of meperidine; on the other hand, delayed neonatal neurobehavioral changes are probably related to the metabolic product normeperidine. Sosa et al. evaluated the association between the use of meperidine during the first stage of labor and the presence, type, and timing of acidosis in the newborn at birth

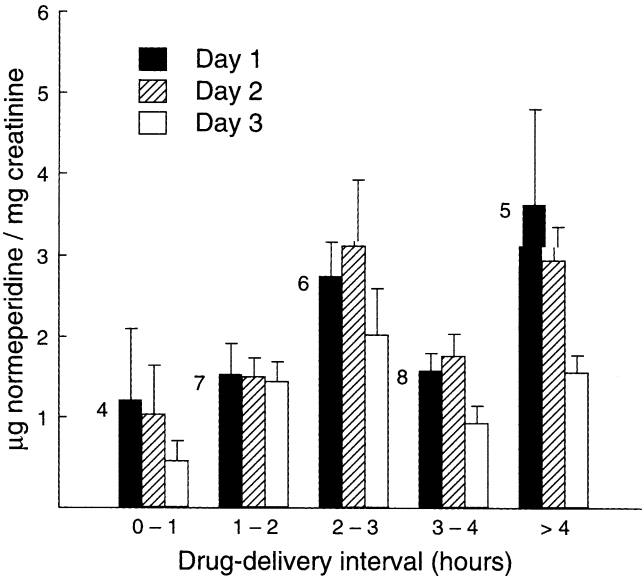

Figure 8–2. Relationship between the meperidine delivery interval and urinary excretion of normeperidine by the neonate. (Adapted from Kuhnert et al.[5])

and found that there was an increased risk of acidosis at birth in the meperidine group as compared to the control group.[6] Neonatal neurobehavioral change has also been observed from normeperidine excreted from breast milk.[7]

Fentanyl

Fentanyl is a rapid-acting and short-lasting narcotic, and 100 µg of fentanyl is equipotent to 10 mg of morphine and 100 mg of meperidine. This agent can be used intramuscularly (50–100 µg) or intravenously (25–50 µg) and will have its peak effect in 7–8 min and 3–5 min, respectively. The main disadvantage of this agent is its short duration: it only lasts for 1–2 h even if used intramuscularly.

Fentanyl can be used via patient-controlled intravenous analgesia (PCIA) technique to provide labor analgesia. In one study,[8] patients received an initial IV dose of 100 μg of fentanyl incrementally over 1–5 min. If the pain was not adequately relieved, an additional 50 μg was given and repeated every 5 min until the patient reported adequate pain relief. The PCIA pump was initially set to give aliquots of 25–50 μg fentanyl with a lockout interval of 10 min. The lockout period and bolus dose were increased or decreased to achieve desired comfort level. Although this technique did not provide better analgesia than conventional patient-controlled epidural analgesia, it offers a good alternative method where a regional anesthesia is contraindicated. Just like any systemic analgesic techniques, intravenous fentanyl produces more maternal and neonatal sedation compared to regional anesthesia.[8] On the contrary, fentanyl administered as single dose does not have significant neonatal effects. Eisele and colleagues used 1 μg/kg of fentanyl intravenously before cesarean section and found no differences in Apgar scores, in umbilical cord acid–base values, or in neurobehavioral scores between medicated and control groups.[9] Recently Frolich et al. also demonstrated that 1 μg/kg of fentanyl and midazolam 0.02 mg/kg given intravenously before the cesarean delivery did not have any adverse neonatal effects (Can J Anaesth 2006;53:79–85).

Remifentanil

Remifentanil, a new ultra short-acting opioid receptor agonist produces analgesia; however, it is quickly metabolized by nonspecific esterases. It crosses the placenta, but it is rapidly metabolized by the neonate. It has been used as a continuous intravenous infusion or patient-controlled infusion with some success.

In one study,[10] 20 term parturients requesting labor analgesia were randomized to receive one of two regimens of intravenous remifentanil. The initial settings in both groups consisted of an infusion of 0.025 μg/kg/min and a PCA bolus of 0.25 μg/kg and a lockout interval of 2 min. In Group A, the infusion was increased in a stepwise manner from 0.025 μg/kg/min to 0.05 μg/kg/min, 0.075 μg/kg/min, and 0.1 μg/kg/min as required; the bolus was kept constant at 0.25

μg/kg. In Group B, the bolus was increased from 0.25 μg/kg to 0.5 μg/kg, 0.75 μg/kg, and 1 μg/kg as necessary; the infusion was kept constant at 0.025 μg/kg/min. Maternal pain, satisfaction and sedation scores, remifentanil requirement, and side effects were recorded. Mean pain and patient satisfaction scores, and cumulative doses of remifentanil were similar in the two groups. The overall incidence of side effects was greater in Group B ($P = 0.0007$), with drowsiness observed in 100% of patients, as compared to 30% in Group A ($P = 0.003$). The minimum oxygen saturation levels were 94.3% +/– 2.6% and 92.2% +/– 3.8% in Groups A and B, respectively ($P = 0.19$). The authors concluded that although pain and satisfaction scores were similar in both groups, the regimen used in Group A was associated with fewer side effects compared to the Group B dosing regimen. However, there is a potential for respiratory depression and mandates close respiratory monitoring. When compared to epidural analgesia, this technique is not superior.[11]

Sedatives and/or Tranquilizers

These agents can be used either to allay apprehension and anxiety or in conjunction with narcotics to decrease the incidence of nausea and/or vomiting.

Barbiturates

Barbiturates are seldom used at the present time because of their adverse effects in neonates when used in high doses.

Phenothiazines

Hydroxyzine (Vistaril) and promethazine (Phenergan) have been used extensively in obstetric cases. These agents possess effective anxiolytic as well as antiemetic properties *and can decrease the beat-to-beat variability of the fetal heart rate.*

Benzodiazepines

These agents are effective anxiolytic, hypnotic, anticonvulsant, as well as amnestic drugs.

Diazepam

A popular anxiolytic drug, diazepam has been used extensively in obstetric practice. In small doses (2.5–10 mg) diazepam did not affect Apgar scores or neonatal acid–base values; however, lower Scanlon neurobehavioral scores were observed at 4 h.[12,13] *In larger doses diazepam can produce neonatal hypotonia, lethargy, and hypothermia.* In the past, diazepam has been used to treat convulsions following local anesthetic toxicity or in eclamptic patients. Midazolam has replaced diazepam for these indications.

Midazolam

Because of its fast onset and short half-life this agent has become very popular in nonobstetric cases. Because of its potent anterograde amnestic effect, one has to be careful when using it for parturients. However, as mentioned above, midazolam, 0.02 mg/kg, in combination with fentanyl, 1 μg/kg given intravenously before the cesarean delivery did not have any adverse neonatal effects. This approach seems to be a good option in very anxious patients prior to cesarean delivery.

Dissociative Medications

In small intravenous doses (10–15 mg) ketamine may be a useful analgesic drug.[14] The onset of action is about 30 s and lasts for 4 min. Bolus doses up to 0.25 mg/kg are suggested.[15] We have occasionally used 0.5 mg/kg bolus intravenous dose followed by 0.5 mg/kg/h infusion in patients to provide labor analgesia where regional analgesia was not an option. This was used in conjunction with fentanyl PCIA. Undesirable hallucinations were minimal. However, the quality of analgesia obviously will not match that from regional analgesia. Nonetheless, ketamine provides another option of systemic analgesia during labor.

Ketamine has been used as an induction agent during general anesthesia for cesarean section. The possibility of delirium and hallucinations during emergence from cesarean section following large doses of ketamine may be a problem. The use of

midazolam during induction can decrease the incidence of this drawback. Other untoward side effects include hypertension, increased salivation, as well as increased involuntary movements. An *increased intensity of uterine contractions has also been observed following the use of ketamine* (*>1 mg/kg intravenously*);[16] neonatal depression can also occur in this dose range.

Amnestic Agents

Scopolamine (hyoscine) is a potent amnestic agent and also possesses mild sedative properties. It was used in combination with morphine for "twilight sleep." Scopolamine crosses the placenta and can cause fetal tachycardia and a loss in beat-to-beat variability.

Neuroleptanalgesia

Innovar (droperidol, 2.5 mg/mL, plus fentanyl, 0.05 mg/mL), although extensively used in general surgical cases, has never become popular in the obstetric population.

Agonist and Antagonist Agents

Butorphanol (Stadol) and nalbuphine are popular at the present time for the relief of labor pain. One to two milligrams of butorphanol has been found to be as effective as 40–80 mg of meperidine for relieving labor pain. Butorphanol was associated with less drowsiness as well as less nausea and/or vomiting. *However, the use of butorphanol was associated with a 75% incidence of transient sinusoidal fetal heart rate pattern.*[17] Because of the problem with the sinusoidal pattern, although benign, as well as maternal somnolence, butorphanol is rarely used at Brigham and Women's Hospital at the present time. Nalbuphine (Nubain), 5–10 mg intravenously, has become the drug of choice. In a double-blind randomized study using intravenous increments of nalbuphine, 3 mg, vs. meperidine, 15 mg, by patient-controlled analgesia during the first stage of

labor, better maternal analgesia was observed with nalbuphine; there were no differences between the two in the maternal or neonatal side effects.[18] The half-life of nalbuphine in the neonate has been estimated to be 4.5 h and therefore the neonatal respiratory monitoring is required in newborns born to mothers receiving nalbuphine for the labor and delivery.[19]

Inhalation Analgesia

Inhalation analgesia is still being used in different parts of the United States and more often in Europe. A survey from Ontario noted that nitrous oxide was available in 75% of hospitals. Hospitals without the availability of epidural analgesia were more likely to have nitrous oxide analgesia than those with epidural analgesia (89% vs. 70%).[20]

In the United Kingdom, inhalation analgesia has been used with great success during both the first stage as well as the second stage of labor. *Entonox is a mixture of 50% oxygen and 50% nitrous oxide and available in cylinders in United Kingdom.* This mixture may be administered by unsupervised midwives in Great Britain in settings where regional anesthesia is not available. The flow of the gases from the cylinder to the mask can be controlled by one-way valve to limit pollution of the labor suite. *One of the main problems with this agent (Entonox) is the possibility of unreliable concentrations being delivered from the Entonox cylinder when the ambient temperature reaches –7°C;* in such a situation, nitrous oxide becomes liquid in the cylinder. Under these circumstances, parturients will inhale 100% oxygen initially, followed by very high concentrations of nitrous oxide, and this can result in maternal hypoxia. Parturients can self-administer this agent; however, constant communication between the woman and the administrator is absolutely vital. One should start to inhale 30 s before the onset of the contraction so that an adequate brain concentration can be achieved at the peak of the uterine contraction. With intermittent inhalation of nitrous oxide, accumulation over time is negligible, and the neonate eliminates most of the gas within minutes of birth.[21]

Besides N_2O, the other inhalation agents that have been used in the past are methoxyflurane, trichloroethylene (Trilene),

enflurane, and isoflurane. Enflurane 1% in oxygen or isoflurane 0.75% in oxygen have been compared with N_2O/O_2 (50%) for relief of labor pain and found to be more effective than N_2O/O_2 mixture.[22,23] More recently, newer inhalational agents with low blood gas solubility, desflurane and sevoflurane, have been trialed during labor and delivery. In one study, the authors compared the efficacy of Entonox with sevoflurane 0.8% during labor and they concluded that self-administered sevoflurane at subanesthetic concentration (0.8%) can provide useful pain relief during the first stage of labor, and to a greater extent than Entonox. Although greater sedative effects were experienced with sevoflurane, it was preferred to Entonox.[24] In another study, the authors compared desflurane (1–4.5%) in oxygen to nitrous oxide (30–60%) in oxygen for labor analgesia. They found that analgesia scores were similar for both groups with more amnesia in desflurane group (23% vs. 0% $P < 0.05$). Blood loss did not differ significantly: 364 ml for the desflurane group and 335 ml for the nitrous oxide group. There were no significant differences for neonatal Apgar score at 1 min or at 5 min or the NACS at 2 h or 24 h between the two groups. Hence, desflurane in subanesthetic doses seems to be safe and effective inhalation agent for normal delivery but might be associated with greater sedation.[25]

The effect of the inhalation agents on uterine activity and neonates will depend upon the concentrations of the agents used. In smaller concentrations, no detrimental effect on uterine contraction or neonates has been observed.

If general anesthesia is ever indicated for vaginal delivery, then one must take all precautions (nonparticulate antacid, preoxygenation, cricoid pressure, endotracheal tube with an inflated cuff) similar to those mandatory during general anesthesia. *Occasionally a high concentration of inhalation anesthetics may be necessary to relax the uterus for manipulation by the obstetrician.*[26,27] *Major indications for these manipulations are (1) extraction of the head during a breech delivery, (2) internal version and extraction of the second baby during the delivery of twins, (3) extraction of a retained placenta, and (4) reduction of uterine inversion.* To minimize postpartum bleeding, one should immediately shut off the inhalation anesthetics following uterine relaxation.

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9
Relief of Labor Pain by Regional Analgesia/Anesthesia

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By far the most popular form of labor pain relief is regional analgesia. A number of techniques are possible for the different phases of labor and are listed in Table 9-1. This chapter will

Table 9–1. Techniques Used for Relief of Labor Pain

First Stage	Second Stage
(1) Epidural analgesia	(1) Epidural analgesia
(2) Continuous spinal analgesia and anesthesia	(2) Spinal anesthesia
(3) Combined spinal-epidural technique (CSE)	(3) Combined spinal-epidural technique (CSE)
(4) Caudal analgesia	(4) Caudal analgesia
(5) Paracervical block	(5) Pudendal nerve block
(6) Bilateral sympathetic block	

focus on central neuraxial techniques, including epidural and combined spinal-epidural analgesia.

Epidural Analgesia

This is the most commonly employed procedure for both the first and second stages of labor. It offers greater benefits when compared with any other anesthetic methods for labor and delivery.

Anatomy of the Epidural Space

Recent cryomicrotome studies of fresh cadaveric specimens have advanced the knowledge of epidural spaces for the anesthesiologist. The epidural space is partially a potential space, in that it is "empty" but the dura and ligamentum flavum are not adherent, so that it may be expanded to accept catheters and drugs. Contents of the epidural space as described by Hogan are contained in a series of "metamerically and circumferentially discontinuous compartments" (parts at each vertebral segment filled with fat and other contents) separated by zones where the dura contacts the canal wall. The dura tapers off inferior to the L4–L5 disc in the sacral canal, and the space is usually filled by the epidural fat.[1] The posterior epidural space is occupied at each segment by a fat pad in the triangular space between the ligamenta flava and dura. Hogan observed no midline fibrous septum. However, the presence of midline fatty tissue can potentially cause uneven spread of local anesthetic and result in a patchy or unilateral block. When unilateral block occurs, it is usually on the right side, though the mechanism of this finding is unclear.[2] The distance from the skin to the epidural space has been observed with graduated needles and by using ultrasound and magnetic resonance examination. The depth varies considerably from 3 cm to 9 cm; the average depth is 4.5–5.5 cm.[3]

The posterior epidural space is triangular in shape, with the apex facing posteriorly (Fig. 9-1), and lies between the dura mater and the ligamentum flavum. The epidural space extends

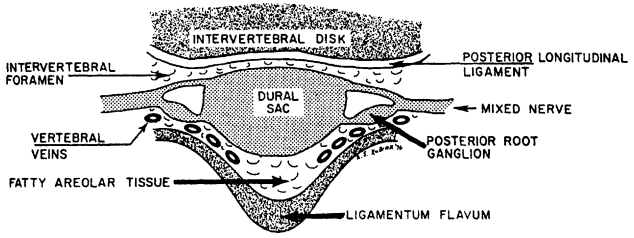


Figure 9–1. Contents of the epidural space. (From Abouleish.[79] Used with permission.)

from the base of the skull to the sacral hiatus *and is bounded* as follows:

1. Superiorly by the dura adherent to the skull at the foramen magnum. The clinical implication of this is related to the absence of total spinal anesthesia via the epidural route.
2. Inferiorly by the sacrococcygeal ligament at the level of the S2–3 interspace.
3. Anteriorly by the posterior longitudinal ligament (lying anterior to the dural sac).
4. Posteriorly by the ligamentum flavum.
5. Laterally by the dural cuffs, pedicles, and lamina.

Contents of the Epidural Space

The epidural space is sometimes characterized as a "potential" space in that it can be expanded by infused local anesthetic. However, the space is not empty prior to the block, and indeed contains several important structures:

1. Anterior and posterior nerve roots with their coverings.
2. Blood vessels that supply the spinal cord.
   a. The posterior spinal artery, which originates from the inferior cerebellar artery and supplies the posterior columns and posterior horns.
   b. The anterior spinal artery, which originates from the two vertebral arteries at the foramen magnum and supplies the anterior portion of the spinal cord.
   c. The artery of Adamkiewicz, which is the major feeder of the anterior spinal artery and arises from one intercostal

or lumbar artery in the T8–L3 region. It supplies the lower two-thirds of the spinal cord.

d. The vertebral veins, which drain blood from the vertebral column and the nervous tissue and ultimately form the vertebral venous plexus. They run via the anterolateral part of the epidural space and ultimately drain into the azygos vein. This venous connection is associated with important clinical implications: *during pregnancy due to obstruction of the inferior vena cava, epidural and azygos vein blood flow is markedly increased. A small dose of local anesthetic injected accidentally into the epidural vein, especially during labor, can reach the heart in a higher concentration*[4] *and thus increase the chances of myocardial depression.*

3. Fatty areolar tissue, deposited between the nervous and vascular structures.

Site of Action

The site of action of the local anesthetic during epidural analgesia is not exactly known; however, several sites have been suggested: (1) spinal roots, the most important site; (2) mixed spinal nerve; (3) dorsal root ganglion; and (4) the spinal cord, which might be the ultimate site of action and plays an important role in regression of a prolonged epidural block.

Techniques

For theoretical purposes, segmental block and complete block techniques have been described; in practice, however, they overlap and form contiguous processes. Segmental block may be used in the first stage to limit the extent of sensory analgesia to the T10–L1 segments. As labor progresses to the second stage, analgesia can be extended to block the sacral innervations. A top-up dose may be required for this purpose while the woman is in the sitting position for about 5 min. If a forceps delivery is planned or if cesarean section becomes necessary, a higher concentration of local anesthetic may be used to achieve motor block and perineal relaxation. In a complete block (T10–S5) sensory analgesia from T10 to S5 is provided

from the very first dose, but theoretically the incidence of hypotension may be higher than when a segmental approach is used.

Epidural Analgesia Procedure

The following materials are needed for epidural placement:

1. An epidural tray (with catheter)
2. Local anesthetic agent: Typically, bupivacaine, 0.0625–0.5%, or ropivicaine 0.1–0.2% (more dilute solutions are popular in present practice); and an epidural infusion, either premixed or prepared from sterile saline solution in a 50- to 100-mL sterile plastic bag. Popular infusions include bupivacaine with fentanyl (0.0625–0.125% bupivacaine with 2 mcg/ml fentanyl).
3. A volumetric infusion pump or commercially available epidural pumps. The latter include important safety features not found on generic infusion pumps.
4. Fentanyl or sufentanil, if no premixed bags of epidural solutions are available, to achieve the final desired concentration (e.g., 2 mcg/ml fentanyl or 0.5 mcg/ml sufentanil)
5. Resuscitative equipment and drugs, including oxygen and delivery apparatus (facemasks, resuscitation bag), oral and nasal airways and endotracheal tubes, laryngoscope, cardiac monitor, induction drugs, and succinylcholine

At the Brigham and Women's Hospital, every effort is made to consult the parturient before induction of epidural anesthesia and informed consent is signed by the patient. Brigham and Women's also provides information via printed booklet and website (www.painfreebirthing.com, or http://www.brighamandwomens.org/painfreebirthing). Depending on the preference of the anesthesiologist, the technique is performed with the patient either in sitting position or in lateral position. One study showed that epidural catheter insertions in the lateral position are associated with decreased incidence of intravascular catheters.[5] The other advantages claimed in favor of lateral position are: *for the mother*, the lateral position is less physiologically demanding and reduces the need to abandon the technique due to vagal reflexes; the lateral position also enables the provision of neuraxial analgesia (and anesthesia) in the event of complex presentation; *for the fetus*, an improvement in blood flow resulting

in better gas exchange.[6] The left lateral position is preferred to the right lateral position as the former is associated with better maintenance of uterine blood flow. The arguments in favor of sitting position include the technical ease of insertion, superior patient comfort, possible improved analgesia for combined spinal epidural (CSE), and decreased aortocaval compression.[7] However, in obese women, physicians at Brigham and Women's, like many others, prefer a sitting position.

Observation of the fetal heart rate is of paramount importance before the introduction of epidural anesthesia. A volume of 500–1,000 ml of Ringer's lactate solution is used for acute volume replacement unless contraindicated, although evidence supporting this practice in preventing hypotension is lacking.[8] Sodium citrate, 30 mL, is given p.o. routinely before the induction of epidural analgesia. At Brigham and Women's Hospital, the Weiss modification of the Tuohy needle is routinely used. About 50% of anesthesiologists in the authors' institution use the technique of loss of resistance by air. Others prefer loss of resistance to saline technique. The superiority of one technique over the other is debatable (Arendt and Segal, Rev Obstet Gynecol 2008;1:49–55). However, using minimal quantities of air or saline to detect epidural space is equally effective. The L2–3 or L3–4 interspace is usually used for introduction of the epidural needle. *Tuffier's line, a line drawn from the top of the iliac crest, coincides with either the L4–5 interspace or the L4 spinous process, though the accuracy of identification of interspaces is quite low.* Once the space is identified by using either the loss-of-resistance to air or saline, 3–5 cm of the epidural catheter is inserted into the epidural space. The length of the catheter inserted into the epidural space depends on the type of catheter as discussed in the following section. Some practitioners prefer not inserting *more than 3 cm of the catheter into the epidural space unless the patient is obese. This technique may decrease the incidence of a unilateral block*.

Multiorifice Versus Uniorifice Epidural Catheters

Multiorifice catheters have recently become increasingly popular as they decrease the incidence of unilateral

blocks.[9–11] Beilin et al. studied 100 women in a prospective, randomized, and double-blind study. Patients were randomly assigned to have a multiorifice epidural catheter threaded 3 cm, 5 cm, or 7 cm into the epidural space. After placement of the catheter and administration of a test dose with 3 mL of 0.25% bupivacaine, an additional 10 mL of 0.25% bupivacaine was administered in two divided doses. Fifteen minutes later, the adequacy of the analgesia was assessed by a blinded observer. The authors found that catheter insertion to a depth of 7 cm was associated with the highest rate of insertion complications while insertion to a depth of 5 cm was associated with the highest incidence of satisfactory analgesia.[12] In another study[13] 800 healthy parturients requesting epidural analgesia were randomized to have open-tip (i.e., single-orifice) epidural catheters inserted 2 cm, 4 cm, 6 cm, or 8 cm within the epidural space. Epidural catheters inserted 8 cm within the epidural space were associated with more intravenous cannulation. Epidural catheters inserted 2 cm within the epidural space resulted in decreased incidence in unilateral sensory analgesia but were more vulnerable for dislodgement during movements of the laboring women. Twenty-three percent of epidural catheters inserted > 2 cm within the epidural space required manipulation. Therefore, if uniorifice catheters are used, the optimum catheter insertion is a balance between a good bilateral block and dislodgement. Based on these studies, some clinicians choose to insert a uniorifice epidural catheter no more than 3–4 cm or a multiorifice catheter no more than 5 cm into the epidural space. Recently, the practice at Brigham and Women's Hospital has changed to using single-orifice soft-tip catheters (open ended Arrow Flex-Tip®) as these catheters decrease the chances of intravascular insertion and the incidence of parasthesia without significantly increasing the incidence of inadequate blocks (when inserted 3–4 cm).[14]

Changes in the Position of Epidural Catheters Associated with Patient Movement

Epidural catheter movement has been noted with change in patient position and can result in inadequate anesthesia. This was investigated by Hamilton et al. in 255 parturients

requesting epidural anesthesia for labor or cesarean section, where a multiorificed lumbar epidural catheter was inserted with the patient in the sitting flexed position.[15] The distance to the epidural space, length of catheter inserted, and amount of catheter position change as the patient moved from the sitting flexed to sitting upright and then to the lateral decubitus position were measured before the catheter was secured to the skin. Data were grouped according to body mass index (BMI): < 25 kg/m^2, 25–30 kg/m^2, and > 30 kg/m^2. Catheters frequently appeared to be drawn inward with position change from the sitting flexed to lateral decubitus position, with the greatest change seen in patients with BMI > 30. Maximum epidural catheter position change was 4.28 cm in a patient in the > 30 BMI group weighing more than 180 kg. Based on these results, the authors recommend that multiorificed catheters be inserted at least 4 cm into the epidural space and that patients assume the sitting upright or lateral position before securing the catheter to the skin.[15]

Test Dose

An ideal test dose should be able to detect both accidental intravascular and subarachnoid injections of local anesthetics. Moore and Batra originally suggested that the use of 15 μg of epinephrine (1:200,000) with local anesthetic will detect accidental intravascular injections in nonpregnant patients by showing tachycardia.[16] The heart rates of the 175 patients increased from a mean of 79 ± 14 beats per minute to 111 ± 15 beats per minute. The heart rate increased within 23 ± 6 s following the injection and returned to baseline within 32 ± 33 s. However, the investigators used this test dose only in nonpregnant cases that were undergoing elective surgery and were under the influence of heavy premedication. When using 3 mL of 0.5% plain bupivacaine via the epidural route in 100 parturients in active labor, Cartwright and colleagues[17] observed heart rate increases of more than 20 beats per minute in 24 women and more than 30 beats per minute in 12 women in the following 60 s even though the catheters were not intravascular. Leighton and colleagues, using 15 μg of epinephrine intravenously in term parturients, observed heart rate increases

of greater than 25 beats per minute that lasted longer than 15 s in only 50% of cases.[18]

From these early studies it appeared that in pregnant women 15 μg of epinephrine might not be sensitive or specific enough to rule out accidental intravascular injection.[19] On the other hand, Abraham and colleagues, in search of an ideal test dose for both accidental intravascular and subarachnoid injections, used 3 mL of 1.5% hyperbaric lidocaine mixed with epinephrine (1:200,000) via an epidural catheter[20] (Fig. 9-2). The maternal heart rate increased from 76 ± 2 beats per minute to 109 ± 6 beats per minute if the solution was injected intravenously, and the sensory anesthesia reached the S2 level in 1.45 ± 0.12 min if the solution was accidentally injected in the subarachnoid space. Hence, the use of epinephrine, 15 μg, for the diagnosis of accidental intravascular injections remains

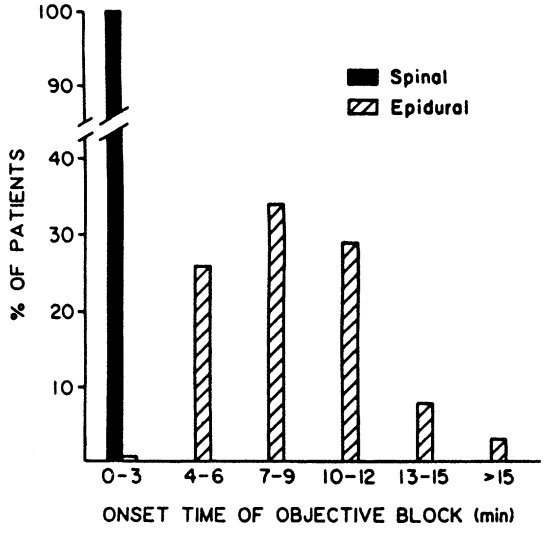


Figure 9–2. Time to onset of objective sensory loss (to pin prick) following epidural and spinal administration of a hyperbaric 1.5% lidocaine solution. (From Abraham.[20] Used with permission.)

controversial. If epinephrine is used in the laboring women as a test dose, one must first observe the maternal heart rate change from base to peak of a uterine contraction. Then one can interpret the effect of intravenous epinephrine.

Other approaches have been advocated. Leighton and colleagues examined air as a useful clinical indicator of intravenous placement of the epidural catheter. Using 1 mL of air through the epidural catheter and monitoring heart tones with a Doppler ultrasound probe, these authors observed only a 2% false-positive rate.[21] None of the 303 parturients in their study developed any complications due to the injection of 1 mL of air; the authors concluded that air, with precordial Doppler detection, is a safe and effective test for identifying intravenously located epidural catheters. This technique was not further evaluated and has not gained popularity in clinical practice. In the meantime, while the search continues for an ideal test dose,[22] one should exercise caution in preventing and diagnosing an incorrect placement of the epidural catheter:

1. For elective cases, unless contraindicated, one can use an epinephrine (15 μg)-containing solution as a test dose. Continuous electrocardiographs (ECG) monitor or pulse oximetry is essential to detect tachycardia. In this respect, one must remember that parturients who are being treated with β-*blocking drugs may not show tachycardia even when the epinephrine is intravascular.*[23]
2. Negative aspiration findings may not exclude intravascular catheter placement because the catheter may be against the vein wall and because aspiration can collapse the vein lumen. Aspiration immediately following the injection of local anesthetic may be more effective in recognizing intravascular catheter placement because the local anesthetic will push the vein wall away and may also dilate the blood vessels; placing the catheter 45–50° below the patient's body level at this stage can help the blood to flow through the catheter if it is intravascular.
3. Local anesthetics should be injected only 3–5 mL at a time, and the signs and symptoms of intravascular injection should be closely monitored. Fractionation of boluses of local anesthetic should prevent toxicity even if there is false-negative test dose.

4. Many anesthesiologists have argued for a no test dose technique in which "every dose is a test dose" and signs and symptoms of intravascular injection are sought every time a bolus of local anesthetic is administered. Brigham and Women's Hospital currently prefers this approach.

Initial Bolus Administration

Initial labor analgesia is generally provided with a variety of local anesthetic agents such as bupivacaine, levobupivacaine, or ropivacaine. At Brigham and Women's Hospital, we typically administer 20 ml of 0.125% bupivacaine for the initial establishment of the pain relief. This is administered in fractionated quantities of 5 ml boluses each. This initial volume can be decreased to 15–17 ml if 3 ml of lidocaine with 15 μg of epinephrine has been used for the epidural test dose. Other institutions favor more dilute initial boluses, such as bupivacaine or ropivicaine 0.1% or less.

Maintenance of Labor Analgesia

After obtaining initial pain relief with fractionated boluses of loading dose of the local anesthetic agent, further analgesia can be provided using intermittent injections or continuous infusion techniques.

Intermittent technique. Reinforcement is needed every 1.5–2 h or if the patient is uncomfortable, with the usual aim to maintain sensory analgesia from T10 to S5.

Continuous analgesia. Can be provided with infusion systems and is a more convenient method for providing satisfactory labor analgesia. A 50–100-mL sterile plastic bag is filled with a 0.0625–0.125% solution of bupivacaine and attached to the high-pressure infusion tubing (Luerlock). The tubing is flushed to remove any air and then connected directly to the epidural catheter. All connections must be secured, and the plastic bag must be labeled. The epidural (or generic volumetric) infusion pump is adjusted to deliver the desired dosage per hour. In the past higher concentrations of local anesthetic drugs, such as bupivacaine 0.25%, were used. The present trend is to use lower concentrations of local anesthetics in

attempt to minimize the motor effects of labor analgesia. Drugs commonly used are bupivacaine or levobupivacaine (0.0625–0.125%) or ropivacaine (0.1–0.2%) at 8–10 mL/h. The marginal differences in effectiveness between these agents are debatable but they all provide adequate analgesia with no significant influence on mode of delivery, duration of labor, or neonatal outcome.[24,25] In some studies bupivacaine has been attributed to more motor block than ropivacaine. However, this is not conclusively proved in other studies and may simply reflect a potency difference between the drugs.[26] In addition to the local anesthetic agents that are in use currently, other drugs such as 1% 2-chloroprocaine and 1% lidocaine have also been used in the past. They can be used under exceptional circumstances.

Continuous infusion for epidural analgesia in obstetrics was first described in 1963.[27] However, the technique did not become popular, mainly because of the lack of availability of proper instruments as well as local anesthetics. With the advent of better mechanical infusion pumps as well as better local anesthetics, continuous infusion has indeed become the technique of choice for vaginal delivery. Different authors have compared the intermittent injection technique with continuous epidural infusion (CEI), and the potential advantages of CEI include[28]:

1. a more stable depth of analgesia, which obviously becomes an important part of patient satisfaction;
2. the possibility of lower blood concentrations of local anesthetic, both by absorption from the epidural space and if the catheter is accidentally placed in the vein;
3. a reduced risk of total spinal block in the presence of an inadvertent injection of local anesthetic in the subarachnoid space;
4. a lower incidence of hypotension due to the possibility of decreased sympathetic blockade

Patient-controlled epidural analgesia (PCEA). PCEA has become popular at the present time[29,30] and is standard practice at Brigham and Women's Hospital. At BWH it is used with a background infusion (bupivacaine 0.125% with fentanyl 2 μg/ml, 6 ml/h, 6 ml patient demand bolus, 15 min lockout between demands, no 4 h limit). This technique offers more

patient control over the level of the block and requires fewer physician interventions compared to the continuous infusion technique.

General considerations during epidural maintenance. During the maintenance phase of labor analgesia with any of the techniques described above, parturients should be positioned head-up with left uterine displacement. Head-up position facilitates adequate perineal anesthesia as the patient progresses from first stage to second stage of labor. Routine monitoring of maternal vital signs, the fetal heart rate, and uterine contractions are essential during this phase. Notations about the block and vital signs should be made every 1–2 h on the hospital record. One must remember that even with the continuous infusion technique one should frequently check the block to verify uniformity and rule out subarachnoid or intravascular migration of the catheter.

Local Anesthetic and Opioid Infusion

A combination of lower concentrations of local anesthetics and lipophilic opioids has popularized CEI and PCEA techniques even further. This combination offers a superior analgesia than local anesthetics alone.[31] Different authors have investigated the efficacy of low concentrations of local anesthetics combined with opioids and have claimed moderate to good success.[32–34] The most popular cocktail at present is the combination of 0.0625% or 0.125% bupivacaine and 2 μg/ml of fentanyl infused at the rate of 8–10 mL/h. Alfentanil (5 μg/mL) has been tried in our institution in combination with bupivacaine (0.125% at 8–10 mL/h) with excellent success. However, placental transfer of alfentanil is significant and hence this drug has never become popular. Sufentanil 0.5 μg/ml is used in some institutions, although no clear advantage has been demonstrated, and it is more expensive. Morphine and hydromorphone, which are more hydrophilic opioids, have not proven satisfactory in labor analgesia (though they may be quite effective after cesarean delivery in larger doses).

Bupivacaine in even lower concentrations of 0.04–0.0625% with opioid has also been tried with varying success; obviously,

the lower concentration will be associated with minimal motor blockade, which might benefit the parturients if the sensory analgesia is adequate.[33] Other local anesthetics such as ropivacaine (0.2%) and levobupivacaine (0.125%) with fentanyl have also been used with success.[24]

Possible Block-Related Problems

Inadequate Perineal Analgesia

At the time of delivery one must make sure of the presence of adequate perineal analgesia. If additional analgesia is deemed necessary, bupivacaine 0.125% (6–8 ml), or 0.25% (3–4 ml) with fentanyl 50–100 μg offers good pain relief for pushing the baby without augmenting the motor block. Placing the parturient in the semi-Fowler's position for "pushing" also helps achieve a more complete perineal block. Additionally, lidocaine 1.5–2%, bupivacaine 0.25–0.5%, or 2–3% 2-chloroprocaine may be required to provide sufficient analgesia or anesthesia if forceps delivery or episiotomy is contemplated.

Asymmetric Sensory Block

If a unilateral block is encountered after initial dosing, the epidural catheter can be withdrawn by 1 cm and in most cases the block will become bilateral after supplemental 3–5 ml of bupivacaine 0.25% or 6–10 ml of 0.125%.[2] If a parturient lies continuously on one side, the level of sensory block may become asymmetric. The situation should be corrected by repositioning the patient, and administering 4–6 mL of 0.25% or 8–12 mL of 0.125% bupivacaine mixed with fentanyl 2 μg/ml solution (bolus dose) after appropriate aspiration, and then the infusion should be restarted. The patient should be encouraged to turn from side to side to maintain uterine displacement.

Diminishing Analgesia

Progressive diminution of the sensory block and loss of the block may be due to a number of factors:

1. The pump on/off switch may be off.
2. The tubing may be disconnected.
3. The reservoir bag may be empty.
4. The catheter may no longer be in the epidural space, and intravascular migration must be ruled out.

The differential diagnosis should consist of rechecking the infusion pump setup and testing to determine the correct position of the catheter. After aspiration, a 3-mL test dose of 1.5–2% lidocaine or 0.25% bupivacaine with or without 1:200,000 epinephrine is injected. The patient is observed for signs of intravascular placement of the catheter, and if there is negative response, an attempt is made to re-establish the block with 3–5-mL incremental doses of 0.125–0.25% bupivacaine. If the block cannot be re-established or if aspiration and testing indicate intravascular migration of the tip, then the catheter must be removed. Depending on the clinical setting, either a new catheter may be inserted via a second placement, or alternative analgesia may be initiated. *At the above infusion rates, bupivacaine probably will not produce symptoms of intravascular injection*. The only clue may be diminishing or absent analgesia.

Dense Motor Block

Patients given a continuous infusion of 0.0625–0.125% bupivacaine usually exhibit mild motor blockade of the lower extremities. If a progressively dense motor blockade resembling a subarachnoid block ensues, the catheter must be disconnected immediately and careful aspiration performed to rule out subarachnoid migration. A suspicion of subarachnoid migration after testing mandates either withdrawal of the catheter and reinsertion at another site or management as a continuous spinal catheter (see below).

Patchy Block

If a spotty or patchy block occurs, one should attempt to solidify the block by aspirating to determine catheter placement and injecting 4–6 mL of 0.125–0.25% bupivacaine. Then

the pump is reconnected. Initially patchy blocks may be due to misplacement of the epidural catheter (subdural, paravertebral, catheter threaded over a nerve root) and consideration of immediate replacement should be given.

Miscellaneous

If a woman requires an acute change in the character of the block for operative delivery, simply increasing the infusion rate will be inadequate. The parturient must be disconnected from the pump, the catheter placement must be checked, and the epidural catheter should then be "topped up" with 0.5% bupivacaine, 2% lidocaine with or without epinephrine, or 3% 2-chloroprocaine to obtain the desired level of sensory anesthesia (to at least a bilateral T4 level for cesarean delivery).

Spinal Anesthesia

Single-shot spinal anesthesia has a very limited role in labor and vaginal delivery. Spinal anesthesia will relax the pelvic floor muscle and will thus disturb the integrity of the birth passage; the expulsive powers can also be diminished by blockade of the abdominal segments. Because spinal anesthesia produces an intense motor block of the pelvic floor muscle, it is a desirable technique for forceps delivery. At Brigham and Women's Hospital, we aim for a T10–S5 block in all forceps deliveries except in the case of a trial of forceps, where we may aim for a higher block (T4) in case cesarean delivery is required. Consultation with the obstetrician regarding the likelihood of success with forceps can help guide the level of anesthesia required. Drugs that can be used are (1) lidocaine, (2) mepivacaine, and (3) bupivacaine.

Continuous Spinal Anesthesia

Continuous spinal anesthesia can be used if there is an accidental or intentional dural puncture. The epidural catheter is inserted 3 cm in the subarachnoid space. Advantages of the

continuous spinal catheter technique include the following: (1) small doses of local anesthetics are needed, (2) rapid onset of action, (3) quick recovery because of the small dose, (4) the absence of accidental intravenous injections of large doses of local anesthetic, and (5) the possibility of the use of small doses of intraspinal opioids for the relief of labor pain in a few special situations. At Brigham and Women's, we administer 2.5–3 mg bupivacaine with 25–30 μg of fentanyl via the spinal catheter as an initial bolus, followed by a continuous infusion of bupivacaine 0.125% with fentanyl 2 μg/ml at 1 ml/h. If the patient becomes uncomfortable during the course of the labor, an additional bolus of 1 ml of the mix or 15–25 μg fentanyl provides comfort. Occasionally, the infusion has to be gradually increased to 2 ml/h in a graded fashion. Since the local anesthetic mixture is hypobaric at body temperature, there is a tendency of inadequate block on the dependent side in lateral positions. This is usually remedied by changing the patient one side to the other before reinforcement with local anesthetic mix.

Combined Spinal/Epidural (CSE)

The CSE technique has become popular since the introduction of neuraxial opioids. The epidural needle is first inserted in the epidural space with loss-of-resistance technique. Then a long pencil-point spinal needle (25- or 27-gauge) is inserted via the epidural needle. This spinal needle usually extends 12 mm beyond the tip of the epidural needle. With the appearance of free-flowing CSF, a mixture of lipid-soluble opioid (fentanyl or sufentanil) mixed with plain bupivacaine is injected via the spinal needle. At this point the spinal needle is withdrawn, the epidural catheter is inserted, and the epidural needle is removed. Different lipid-soluble opioids have been tried; 10 μg sufentanil or 25 μg of fentanyl are most popular. The advantages of CSE may include (1) faster onset of analgesia, (2) decreased or nonexistent motor blockade, (3) less cardiovascular instability, (4) lower amount of local anesthetic in the systemic circulation, (5) shorter first stage

of labor in nulliparous women compared to CEI technique, and (6) improved analgesia when administered in advanced labor.[35,36]

Continuous epidural anesthesia, or PCEA, can be started once the expectant mother is comfortable. No loading boluses are needed. However, if the patient is not comfortable, additional epidural boluses should be administered cautiously because of the possible synergistic effect of the local anesthetic and opioid.

Side effects of CSE technique include:

(1) Pruritus, usually mild and short-lasting. If severe, intravenous nalbuphine (Nubaine) in 5–10 mg doses can be given. Small doses of nalaxone (40–80 μg) or propofol (10 mg) also have been used with success. Eight milligrams of ondansetron has also been used successfully for spinal opioid-induced pruritus.[37]
(2) Nausea and/or vomiting. Less lipophilic morphine may be associated with higher incidences of this side effect.
(3) Respiratory depression is extremely rare with lipophilic opioid.
(4) Fetal bradycardia may be associated with CSE technique.[38] The mechanism is not understood at present. Postulated mechanisms include:
    1. Decrease in maternal epinephrine concentrations; unopposed norepinephrine effect may be associated with increased uterine tone or uterine vessel (macro and micro) vasoconstriction and hence increased uterine tone.[39,40]
    2. Maternal hypotension also may decrease uteroplacental perfusion.
    3. Finally, direct vagotonic effect of the sufentanil on the fetus has been suggested; however, this effect may be just theoretically important.

Treatment should include intravenous ephedrine to increase maternal cardiac output; if the FHR does not improve tocolytic agents (intravenous terbutaline, nifedipine, or nitroglycerin) should be considered. Occasionally urgent delivery may be required in persistent cases.

Monitoring Following Administration of Regional Analgesia

The blood pressure and pulse rate are routinely noted by the nursing staff before and immediately after the induction of anesthesia. Blood pressure is measured every minute for the first 5 min and every 3–5 min thereafter up to 30 min. If the blood pressure remains stable after 30 min, the nursing staff monitors the blood pressure routinely every 15 min throughout labor and delivery. Routine pulse rate measurements are made during the time of blood pressure readings. Continuous pulse oximetry may also be an important tool in selected cases (maternal cardiovascular or respiratory disease, maternal somnolence). In most high-risk pregnant women (e.g., diabetes, preeclampsia) or if there is any sign of fetal distress, a oxygen mask should be used with high-flow oxygen where indicated. Continuous fetal heart rate monitoring becomes absolutely essential after the administration of epidural analgesia. If the parturient complains of tinnitus, circumoral numbness, a metallic taste, dizziness, high sensory anesthesia, or excessive motor blockade, the nursing staff should immediately inform the anesthesiology team for possible migration of the epidural catheter into either the vascular or subarachnoid space.

Contraindications

Besides the usual contraindications for regional anesthesia (e.g., local infection, coagulation problems), continuous infusion or PCEA should be used carefully in a patient with an accidental dural puncture. Frequent checks for excessive sensory and motor block should be performed. If high block is recognized, the infusion rates should be decreased appropriately. In the past, epidural placements were contraindicated if platelet count is below 100,000/mm^3. However, recent techniques of studying coagulation using thromboelastography have shown that the coagulation status is not altered even with lower platelet counts.[41,42] It is presently accepted as reasonable practice to administer epidural anesthesia if platelet counts are above 70,000/mm^3, provided there is no other coagulation abnormality.

Complications of Regional Analgesia

Major anesthesia-related neurological problems are extremely rare; the rate may vary from 1:40,000 to 1:100,000.[43] Obstetric-related major complications are much more common, varying between 1:2600 and 1:6400.[44]

Paresthesia

The incidence of transient paresthesia varies from 5% to 25%. If paresthesia persists, the catheter should be removed and reinserted in another space. Modern soft-tipped epidural catheters (e.g., the Arrow Flex-Tip®) are associated with a lower incidence of paresthesia. The incidence of persistent paresthesia lasting for 4–6 weeks varies between 5 and 42.3 per 10,000 (see Table 9-2).[45] The causal relationship between transient paresthesia during catheter insertion and serious neurologic injury is controversial but it appears to be a significant association.[46]

Table 9–2. Incidence of Paresthesia After Epidural Anesthesia*

Source	Number of Cases	Incidence per 10,000
Crawford	2,035	14.7
Eisen et al.	9,532	16.8
Abouleish	1,417	42.3
Lund	10,000	5.0
Bonica et al.	3,637	24.7

From Ong et al.[45] Used with permission.

Accidental Dural Puncture

The incidence of dural puncture varies among institutions, which may relate to practitioner experience or supervision, characteristics of the patient population (e.g., prevalence of obesity), and equipment and techniques used. The incidence at the Brigham and Women's Hospital is between 1% and 2%. Dural puncture by the epidural catheter is very rare; however, the clinical implication of this is important because of

the possibility of total spinal anesthesia. Post-dural puncture headache (PDPH) is the most frequent complication, with a rate varying from 76% to 85% and which appears to have been consistent over several decades of experience.[47,48]

Treatment of Headache Following Accidental Dural Puncture

Following an accidental dural puncture, the anesthesiologist usually places the epidural catheter in a different space. One should exercise caution while injecting local anesthetic via this newly placed catheter because of direct connection with the dural hole as well as seepage of a small amount of local anesthetic via the dural hole. Alternatively, an epidural catheter may be threaded into the intrathecal space and continuous spinal analgesia may be employed for labor. This maneuver may reduce the incidence of headache, although there is considerable controversy. Other measures to prevent or treat PDPH include epidural saline, prophylactic blood patch, and therapeutic blood patch.

Conservative Management

Women are informed about the occurrence of an accidental dural puncture. Although patients often feel better while not upright, absolute bed rest is not mandatory (Fig. 9-3). Women are advised to drink liberal quantities of fluids, although there is no convincing human data to prove that this reduces headache symptoms. At BWH, most clinicians prescribe analgesic tablets (e.g., acetaminophen/caffeine/butalbital [Fioricet™], or acetaminophen with hydrocodone) if there is a headache. Some have advocated abdominal binders, though there is limited data on effectiveness, and this treatment is impractical if there is an abdominal incision.

Epidural Saline

At the termination of the procedure, several investigators have suggested the use of preservative-free normal saline via the epidural catheter (1) in a single dose (60 mL),[49] (2) every

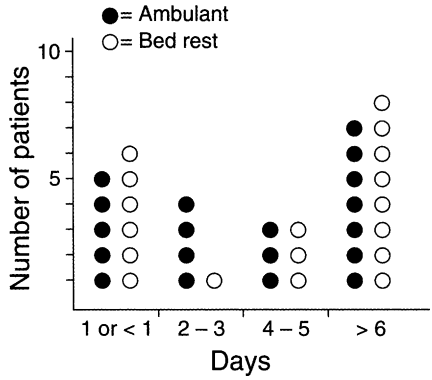


Figure 9–3. Difference in incidence of spinal headache between patients who are ambulatory and on bed rest. (From Carbalt and VanCrevel.[80] Used with permission from Elsevier.)

6 h (30–60 mL),[50] and (3) as a continuous infusion of 1,000 mL over a 24-h period.[51] The success rate has varied considerably.

Prophylactic Blood Patch

A prophylactic blood patch has been used with some success.[52] However, the ultimate validity of this technique is controversial, and a randomized trial failed to show any reduction in PDPH.[53] In our experience, efficacy has been poor, and the majority of the anesthesiologists have abandoned the technique.

Therapeutic Blood Patch

A therapeutic blood patch is indicated (1) if the headache is postural and does not improve within 48 h; (2) if there is severe or debilitating headache limiting activities of daily living or infant care (for example, if accompanied by nausea and vomiting); (3) if there is *blurred vision or diplopia that is related to stretching of the sixth cranial nerve (abducens), which supplies the lateral rectus muscle of the eye;* and (4) if there is hearing

loss following dural puncture, which occurs rarely. Blood patch is contraindicated in the presence of any untreated coagulopathy, fever of unknown origin or untreated systemic infection, or localized infection at the injection site.

Procedures for the use of therapeutic blood patches are as follows:

1. An intravenous catheter is inserted and hydration begun if the patient has not been consuming liberal oral fluids. Overhydration should be avoided, because it will cause a need to urinate and require ambulation.
2. The woman's back is aseptically prepared.
3. If there is only one puncture, then the same interspace is selected; however, if there are multiple punctures, one should use the lowermost interspace because it is easier for epidurally injected blood to spread cephalad than caudad.[54] Some advocate loss of resistance by saline to prevent further intensification of the headache by introducing air through the dural hole. Others emphasize using the technique most familiar to the operator, but care should be taken not to inject significant air into the epidural space.
4. Once the epidural needle is positioned properly, blood should be drawn from a large vein (20–30 ml) after proper aseptic care.
5. Blood should be injected slowly until patient feels consistent pressure in the back.
6. The woman should lie supine with pillows under the knees for 1–2 h.
7. The woman should be monitored carefully for a few days. Strenuous activity and extreme bending of the back should be avoided for 24–48 h. Modest back pain is common for the first day and may be treated with nonsteroidal anti-inflammatory drugs.

The incidence of success from the first blood patch has been observed to be as high as 70–75%; in a few cases, a second or third blood patch may be necessary. The most common causes of failure of the blood patch are wrong diagnosis and improper placement of the patch. If the blood patch fails, one has to re-evaluate the diagnosis, and if necessary, a neurologist should be consulted. Cortical vein thrombosis, which mimics symptoms after a dural puncture, has to be excluded because a blood

patch can make the clinical condition worse. CT scans may confirm the diagnosis.[55]

Experimental and Alternative Techniques

Recently, alternative techniques for the treatment of post-dural puncture headache have been reported. In one study,[56] a prospective, randomized, double-blind trial was conducted to study the effect of epidural morphine in prevention of post-dural puncture headache in 25 parturients after inadvertent dural puncture. Women were randomly allocated to receive two epidural injections, 24 h apart, of either 3 mg morphine in 10 ml saline (morphine group) or 10 ml saline (saline group). The incidence of headache and need for therapeutic epidural blood patch were reported. There was a significant difference in the incidence of headache between the two groups: 3/25 (12%) in the morphine group and 12/25 (48%) in the saline group ($p = 0.014$). Therapeutic epidural blood patches were required in six patients in the saline group and none of the patients in the morphine group ($p = 0.022$). Another group reported the use of intravenous hydrocortisone 200 mg, followed by 100 mg three times daily for 48 h decreased the intensity of headache following post-dural puncture as compared to the control group (bed rest, acetaminophen, meperidine, and fluids).[57] Anecdotal success has also been reported with adrenocorticotrophin (ACTH) 80 i.u. administered intramuscularly in the treatment of dural puncture headache.[58]

Subdural Injection

This involves an injection of local anesthetic between the dura mater and arachnoid; because of decreased compliance of this space, a higher spread is possible in comparison with epidural anesthesia. The following are characteristics of subdural injection:

1. Incidence, 0.1–0.82%
2. Incidence increased during rotation of the epidural needle after a loss of resistance
3. Incidence increased in patients with prior back surgery

4. Widespread sensory anesthesia with the use of a small amount of local anesthetic
5. Block usually weak and patchy and spread mainly in a cephalad direction
6. Delayed onset of 10–30 min
7. Hypotension possibly the initial symptom
8. Faster resolution, in comparison with epidural or subarachnoid blockade

Treatment is supportive as the block resolves, and in most cases the catheter must be replaced.

Massive Epidural Analgesia

This represents an excessive segmental spread from a relative overdosage of local anesthetic. This problem is more often seen in morbidly obese individuals as well as in parturients with severe arteriosclerosis and diabetes. The onset of this problem is more gradual, and very rarely does it spread high enough to produce unconsciousness. Treatment is supportive while the block recedes (airway, ventilation, blood pressure). With careful dosing and confirmation of an epidural position, the catheter may continue to be used.

Accidental Intravascular Injection

An accidental intravascular injection of local anesthetic can happen either at the time of induction of epidural analgesia or anesthesia or as a result of subsequent migration of the epidural catheter in the intravascular space. Injection of local anesthetic directly into an epidural vein can give rise to a systemic reaction causing convulsions as well as possible cardiovascular collapse. Initiation of immediate management is important:

1. Assure left uterine displacement.
2. Airway patency must be maintained, if necessary, by an endotracheal tube and ventilation with 100% oxygen.
3. Convulsions are usually short-lived, but if they continue, benzodiazepines (diazepam 5–10 mg, midazolam 1–2 mg, or lorazepam 0.5–1 mg) or a small amount of thiopental (50–100 mg) are indicated.

4. Fetal heart rate monitoring will ultimately govern the next step: if the fetal heart rate is normal, labor can continue for a vaginal delivery, but in the presence of a non-reassuring tracing, an immediate cesarean section with general anesthesia should be planned, and active resuscitation of the fetus may be necessary.

Cardiovascular toxicity of local anesthetics may also occur, particularly with lipophilic drugs (e.g., bupivacaine).

Methemoglobinemia

This rare condition is associated with prilocaine especially when the dose exceeds 600 mg. It can also be associated with topical benzocaine. These drugs are rarely used in modern obstetric anesthesia practice. Treatment includes 1 mg/kg of methylene blue, a reducing agent which restores hemoglobin to the normal ferrous state.

Broken Epidural Catheter

The exact incidence is not known. Most authors advise that a broken catheter be left in place if it is in the lumbar epidural space.[4] Studies in cats showed that implanted epidural catheters were ultimately covered with fibrous tissue after about 3 weeks.

Shivering

The cause of this common event (20–35%) is unknown; however, this side effect can be treated with epidural sufentanil or intravenous or epidural meperidine.

Horner's Syndrome

Although rarely of clinical significance, at least some signs occur in 25–75% of parturients who receive high blocks, for example, for cesarean delivery. The incidence is likely lower in labor analgesia, though obstetric patients may experience it even after volumes of local anesthetic typical of such blocks.[59] Nerves involved are the upper four thoracic nerves, which form

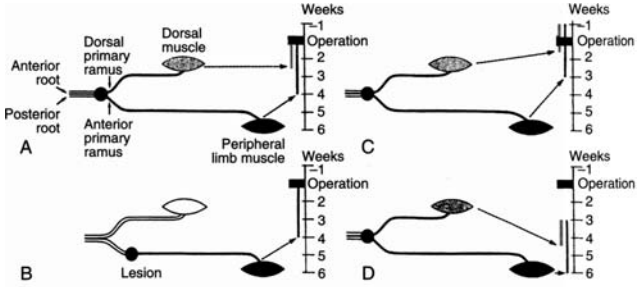
the cervical sympathetic ganglion. Signs include ptosis, miosis, anhydrosis, enophthalmos, and ecchymosis.

Backache

This is a frequent problem following delivery in obstetric patients, occurring in approximately 40% of postpartum women. Multiple attempts with needles may cause temporary localized back pain at the injection site by causing direct trauma and hemorrhage into the intervertebral ligament and vertebral periosteum. More diffuse and longer-lived pain is more common, even after uneventful regional anesthesia. Preexisting conditions like arthritis or osteoporosis may exacerbate the problem. Importantly, however, epidural analgesia does *not increase this risk of ongoing back pain*. Breen et al. observed the incidence of back pain 1–2 months postpartum was similar in parturients with or without epidural analgesia (44% vs. 45%).[60] A similar study followed women for up to 1 year. The authors observed no increased risk of back pain in women who had used epidural analgesia compared with those who did not (10% vs. 14%).[61]

Major Neurologic Injury

Neurological complications in the obstetric population must be divided into obstetric causes and anesthesia-related causes. Anesthesiologists are often requested to consult postpartum women with neurological problems even if these problems are unrelated to regional anesthesia. A clear clinical picture is absolutely necessary to make a proper diagnosis. The following steps will help with the differential diagnosis: history, physical examination, X-ray films, coagulation studies, electromyography to possibly define the timing of the lesion (Fig. 9-4), computed tomographic (CT) scans, and magnetic resonance imaging (MRI). The authors suggest a neurological consultation for any woman with a complicated neurological deficit that does not resolve within a reasonable period.



Electromyography in differential diagnosis of postoperative neurological complications. Diagram of spinal roots, dorsal and anterior primary rami, and peripheral nerves.

Symbols:

●= Lesion

= Normal dorsal (paraspinal) muscle

= Denervated dorsal muscle

= Denervated peripheral limb muscle

= Normal nerve

= Damaged nerve distal to lesion

Vertical scale shows elapsed time in weeks from time of lesion to appearance of denervation EMG patterns in muscles.

A, Lesion of spinal roots at time of operation. Dorsal muscles show EMG changes 1½ weeks later. Distal limb muscles show EMG changes three weeks later.

B, Lesion of peripheral nerve at time of operation. No change in dorsal muscle. Distal limb muscles show EMG changes three weeks later.

C, Associated but unrelated lesion of spinal roots one week before operation.

D, Lesion of spinal roots occurring two weeks after operation.

Figure 9–4. Electromyography in the differential diagnosis of postoperative neurological complications. (Adapted from Bromage, p. 703.[4] Used with permission.)

Obstetric Causes

The incidence of neurological complications related to obstetric causes varies from 1:2,600 to 1:6,400.[62,63] These neurological complications are often associated with prolonged labor and forceps delivery. Changes in the obstetric practice of difficult deliveries might have decreased the incidence of major obstetric-related neurological complications.[45] Peripheral nerves that might be involved include (Table 9-3):

Table 9–3. Neurological Complications Unrelated to Regional Anesthesia: Obstetric Cause

	Clinical Findings	
Nerve	**Sensory deficit**	**Motor deficit**
Lumbosacral trunk (L4, L5)	Hypoesthesia of the lateral aspect of the calf and foot	Weakness of the hip abductor Foot drop Unilateral weakness of the quadriceps
Femoral nerve (L2, L3, L4)	Hypoesthesia of the anterior aspect of the thigh and medial aspect of the calf	Quadriceps paralysis
Lateral femoral cutaneous nerve (L2, L3)	Numbness of the anterolateral aspect of the thigh	
Sciatic nerve (L4, L5, S1, S2, S3)	Pain in posterior gluteal region with radiation to the foot	Inability of flexion of the leg
Obturator nerve (L2, L3, L4)	Decreased sensation over the medial aspect of the thigh	Inability to adduct the leg
Common peroneal nerve (L4, L5, S1, S2)	Sensory deficit over the anterolateral aspect of the calf and dorsum of the foot and toes	Plantar flexion with an inversion deformity
Saphenous nerve (L2, L3, L4)	Loss of sensation over the medial aspect of the foot and anteromedial aspect of the lower portion of the leg	
Lumbosacral plexus (L1, L2, L3, L4, L5, S1, S2, S3, S4)	Variable	Variable

1. A prolapsed intervertebral disk may occur because of the exertional efforts of labor. This may cause spinal root compression, the incidence of which has been documented to be 1 in 6,000 deliveries.
2. The lumbosacral trunk (L4, L5) may be compressed between the descending fetal head and the ala of the sacrum. It might be associated with the use of mid-to-high forceps. Clinical findings may include foot drop, hypoesthesia of the lateral aspect of the foot and calf, a slight weakness of hip adductors, and quadriceps weakness.
3. The femoral nerve (L2, L3, L4) can be injured in the lithotomy position because of hyperacute hip flexion as well as the use of retractors during cesarean section. There will be impaired knee extension due to quadriceps paralysis, an absence of the patellar reflex, and hypoesthesia of the anterior portion of the thigh and medial aspect of the calf.
4. The lateral femoral cutaneous nerve (L2, L3) can be injured by retractors during cesarean section or during incorrect lithotomy positioning. In addition, palsy of this nerve, known as meralgia paresthetica, occurs spontaneously in many women in the third trimester, from musculoskeletal changes of pregnancy. There will be transient numbness of the thigh at the anterolateral aspect.
5. The sciatic nerve (L4, L5, S1, S2, S3) can be injured by incorrect lithotomy positioning along with knee extension and external hip rotation. There will be pain in the gluteal region that radiates to the foot and an inability to flex the leg.
6. The obturator nerve (L2, L3, L4) may be injured due to lithotomy positioning. Acute flexion in the thigh to the groin area, particularly in an obese woman, may lead to compression and cause weakness or paralysis of the thigh adductors.
7. The common peroneal nerve (L4, L5, S1, S2) may be involved in a pressure injury during lithotomy positioning as a result of prolonged compression of the lateral aspect of the knee. The woman may have difficulty standing from a seated position. There will be associated foot drop.
8. The saphenous nerve (L2, L3, L4) can be affected during lithotomy positioning. There will be a loss of sensation over

the medial aspect of the foot and anteromedial aspect of the lower portion of the leg.

9. The lumbosacral plexus (L1, L2, L3, L4 [portion], L5, S1, S2, S3, S4 [portion]) can be injured by the descending fetal head compressing it against the sacrum, particularly in women with unfavorable pelvic anatomy or a large baby. In addition, forceps and retractors during cesarean delivery can compress the plexus. These injuries present with greatly varying sensory and motor deficits, reflecting the site of injury between the nerve roots and the peripheral nerves. When an injury appears not to follow a specific nerve distribution nor be confined to a single root, a plexus injury should be suspected.

Anesthesia-Related Causes

Regional anesthesia used for the relief of labor pain or cesarean section is associated with certain neurological problems. The incidence of motor deficits after the epidural technique varies from 0 to 15/10,000, with the largest studies demonstrating rates of approximately 1/10,000 (Table 9-4).

Prolonged neural blockade. Delayed recovery following epidural analgesia for labor has been described. This was usually associated with the use of tetracaine or bupivacaine in high doses or concentrations. Patchy sensory anesthesia and motor deficit occasionally may last as long as 10–48 h but will ultimately resolve.[64] The etiology of this problem is unknown and may be related to individual patient variation, total dose of local anesthetic used, or physiologic changes of pregnancy altering the pharmacokinetics of the drugs.

Bladder dysfunction. Overstretching of the bladder due to prolonged continuous epidural blockade can produce this problem. Longer-acting local anesthetics are more often associated with this complication, as is intrathecal or epidural morphine. Many labor units routinely place urinary catheters once epidural analgesia has begun.

Trauma to nerve roots. Direct trauma by the needle and catheter to the nerve root is extremely rare, but if it occurs,

Table 9–4. Incidence of Neurologic Deficits Following Epidural Analgesia

First author	Year	Number of cases	Incidence per 10,000
Bonica	1957	3,637	2.7
Lund	1962	10,000	1
Hellman	1965	26,127	0
Dawkins	1969	32,718	Transient, 14.7; permanent, 2.1
Crawford	1972	2,035	0
Moore	1978	6,729	0
Bleyaert	1979	3,000	0
Abouleish	1982	1,417	14.1
Ong	1987	9,403	0.8
Scott	1990	505,000	0.75 (1 case permanent)
Scott	1995	108,133	4.3
Auroy	1997	30,413	2
Aromaa	1997	170,000	0.4
Paech	1998	10,995	0

Adapted from Ong et al.[45] and Munnur U, Suresh MS[81]

it can lead to paresthesia, sensory, or motor loss with a specific dermatomal distribution. Intraneural injections may create neuritis followed by paresthesia lasting weeks to months.

Cauda equina syndrome. This occurs rarely and is characterized by lower extremity and perineal numbness, sphincter dysfunction, and various degrees of lower extremity paralysis. Several cases of neurological problems very similar to cauda equina syndrome following the unintentional spinal (subarachnoid) use of 2-chloroprocaine were described in 1980.[65] Gissen and colleagues[66,67] suggested several factors to explain this problem: (1) the large volume of 2-chloroprocaine injected in the epidural space in the presence of an accidental dural puncture could cause anterior spinal artery syndrome due to increased intraspinal pressure as well as hypotension, and (2) a low pH with a high concentration of the preservative bisulfite can cause neural damage, at least in vitro. However, the bisulfite-pH mechanism has been challenged, and some have argued that chloroprocaine itself may be neurotoxic.[68]

Conversely, there are recent reports of safe use of preservative-free chloroprocaine in human spinal anesthesia.[69]

Another cause of cauda equina syndrome is 5% hyperbaric lidocaine given via spinal microcatheter. The mechanism might be related to high doses of lidocaine that cause nerve damage because of improper mixing with cerebrospinal fluid.[70] Microcatheters were removed from the market in the US in 1991 but are still used in other countries. A large randomized trial recently demonstrated the safety of such devices when appropriate drugs were used (excluding concentrated lidocaine).[71]

Transient neurologic symptoms. A more recently appreciated anesthesia-related neurologic problem that has stirred controversy is transient neurological symptoms (TNS; formerly transient radicular irritation, or TRI). This problem, first described by a group from Switzerland, is characterized by (1) aching pain in the buttocks radiating to both dorsolateral sides of the thigh and calves; (2) association with subarachnoid lidocaine; (3) short duration of symptoms of less than 4–6 days; and (4) surgery in the lithotomy position.[72] Subsequent studies observed that TNS was observed in 30% of cases with 5% hyperbaric lidocaine, 3% with use of 2% hyperbaric prilocaine, and 0% with 0.5% hyperbaric bupivacaine.[73] Interestingly, the incidence of TNS increases significantly when the lithotomy position is used compared to the supine position (13% vs. 5%) with lidocaine, but does not differ between concentrations of lidocaine or addition of dextrose.[74] More recent studies confirmed no difference in the concentrations of lidocaine in the manifestation of TNS in patients undergoing surgery in the lithotomy position.[75] The lithotomy position may stretch L5–S1 nerve roots, which remain in the most dorsal position in the spinal canal. Under this condition, blood perfusion of the nerves or a subset of nerve fibers may be hampered and thus increase the vulnerability to injury. However, careful neurologic studies in volunteers demonstrate no evidence of direct nerve injury in patients developing TNS.[76] Hence TNS is controversial; judicious care is required with the use of drugs that may increase the incidences of TNS.

Epidural hematoma. This is very rare following regional anesthesia, but it may happen following trauma to epidural blood vessels, especially if the clotting parameters are abnormal due to the use of anticlotting medications or because of associated medical problems such as severe preeclampsia or HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome. An *immediate diagnosis is necessary, and surgical decompression should be performed within 6 h.*

Epidural abscess and meningitis. Although extremely rare, infection in the spinal canal is usually secondary to infection elsewhere in the body. Four important clinical features include (1) severe back pain, (2) local overlying tenderness, (3) fever, and (4) leukocytosis. Some case reports of epidural abscess have been reported and found to be caused by skin flora, and rarely meningitis has been traced to oral commensals in the anesthesiologist. Meticulous attention to aseptic technique is mandatory.[77] One should avoid regional anesthesia, if possible, in the presence of untreated bacteremia or septicemia. Antibiotic pretreatment appears to be protective in animal models.[78]

Adhesive arachnoiditis. This can take place as a result of clinical irritation of the structures in the subarachnoid space due to contamination of spinal needles or solutions. Observed symptoms include headache, nausea and vomiting, nuchal rigidity, fever, and Kernig's sign.

Anterior spinal artery syndrome. This is an extremely rare complication in which the anterior part of the spinal cord experiences ischemic degeneration associated with motor deficit. This portion of the cord is more vulnerable because of its single arterial supply as well as lack of collateral supply. Hypotension and unfavorable anatomy are risk factors.

Other Methods of Regional Anesthesia

These techniques are largely of historical interest, though some may occasionally still be used in lieu of modern epidural and spinal techniques.

Caudal Anesthesia

The caudal space is the lowermost part of the epidural space and lies in the sacral canal. This technique involves the introduction of a 17-gauge epidural or 19-gauge 3.8–7.6-cm needle. A catheter can be introduced for continuous use, or a one-shot technique can be used just before the delivery for perineal analgesia. This technique has become unpopular because of the requirement of higher doses of local anesthetics.

Paracervical Block

This technique involves blocking nerve impulses from the uterine body and cervix by injecting local anesthetics in the paracervical tissues. Usually it is performed during the first stage of labor. A paracervical block does not relieve the perineal pain. A continuous technique has also been attempted. This technique is rarely used at the present time mainly because of its depressant effects on the fetus. *Fetal bradycardia following a paracervical block is mainly due to two factors: (1) constriction of uteroplacental blood vessels by local anesthetic and (2) vascular absorption of a large amount of local anesthetic that will directly depress the fetal myocardium.*

Lumbar Sympathetic Block

This technique is technically cumbersome, requires special skill, must be performed bilaterally to be effective, and therefore is seldom used at present; it is useful *only for the first stage of labor.*

Pudendal Block

A pudendal block is performed by the obstetrician just before the delivery by blocking the pudendal nerves while passing over the ischial spine. This technique will provide analgesia of the perineum and is useful only for second-stage labor. In selected cases of unblocked sacral nerves, it may find a place in modern practice even when an epidural block is employed.

Uptake of local anesthetic from this technique is very similar to that in an epidural block.

Summary

Epidural and combined spinal-epidural analgesia are the most commonly employed techniques for labor analgesia. Although very safe and usually quite effective, adequate safety preparations, careful technique and knowledge of potential problems and how to address them, and awareness of possible complications are necessary for the provision of these popular procedures.

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10
Effects of Epidural Analgesia on Labor and the Infant

Properly conducted epidural analgesia is generally quite safe and effective. However, even in the absence of complications, epidural blockade can have effects on the course of labor and on the baby. Regional anesthesia can affect the fetus indirectly through alterations in uterine perfusion and directly through placental transfer of drug. These effects are discussed in Chapters 3 and 5 . This chapter discusses the three most important additional phenomena: effect on the progress of labor and mode of delivery, effect on maternal temperature, and effect on breastfeeding.

Epidural Analgesia and Progress of Labor

There exists considerable controversy over the effect of regional anesthesia on the duration of labor and the mode of delivery. Numerous studies over the last two decades have helped clarify some of the effects.

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Methodological Difficulties

One reason why clear answers to the effects of epidural analgesia remain elusive is the difficulty in studying them. Retrospective studies compared women who self-selected epidural analgesia to those who did not introduce selection bias, because many characteristics of patients requesting epidural analgesia independently predict longer labor and nonspontaneous delivery. These include[1]:

- Nulliparity
- Tendency to come to the hospital earlier in labor and with higher fetal station
- Slower cervical dilation prior to analgesia
- More frequently already receiving oxytocin for induction or augmentation of labor
- Deliver larger babies
- Have smaller pelvic outlets
- May have received epidural analgesia due to other perceived risk factors for operative delivery such as poor fetal status or maternal systemic disease.

Also, recent studies demonstrate that women experiencing more pain in labor, and therefore more likely to request an epidural, are less likely to deliver spontaneously.[2] Conversely, randomized trials have suffered from many problems as well:

- No placebo controls, for ethical and practical reasons
- Opioids used as a control may affect labor themselves
- Blinding is impossible, and unblended obstetricians make the decisions regarding need for cesarean or forceps delivery
- Small sample sizes
- Protocol noncompliance: many women do not stay in randomly assigned group

Initiation of the Block

Some earlier observational studies suggested that early initiation of epidural analgesia (less than 5 cm dilation) was associated with longer labor and an increased risk of cesarean delivery.[3,4] However, randomized trials comparing earlier to later initiation of the block (typically at first request of analgesia vs. $\geq$ 5 cm dilation) have shown no difference in

the length of labor or mode of delivery.[5,6] The American Society of Anesthesiologists (ASA) and the American College of Obstetricians and Gynecologists (ACOG) both recognize maternal request as sufficient indication for initiating labor analgesia.[7] ACOG no longer recommends delaying epidural analgesia to 4–5 cm dilation as it previously did.[8]

Duration of Labor

There may be a transient decrease in frequency of uterine contraction following initiation of epidural analgesia. A plausible mechanism is a reflex decrease in oxytocin secretion from the posterior pituitary due to acute volume expansion.[9] Older studies suggested an effect of epinephrine on uterine contraction perhaps related to a β_2-adrenergic agonist effect, though lower concentrations (e.g., 1:300,000) did not demonstrate any effect.[10,11] Epinephrine-containing solutions for labor analgesia are less popular in modern practice. Once in established labor, the effect of epidural analgesia is minimal. Meta-analysis of nine randomized trials studying over 2,000 women found no significant difference in the length of the first stage (mean [95% confidence interval], 24 min [-19-67], NS). The second stage was slightly prolonged, by 16 (7.5–24) min.[12] Oxytocin use for augmentation of labor is also increased.[13]

Instrumental Vaginal Delivery (Forceps, Vacuum)

The relationship between epidural analgesia and forceps deliveries is complex. The incidence of instrumental vaginal deliveries may be increased by epidural analgesia, although this practice varies tremendously among obstetricians and hospitals. Meta-analysis of randomized trials found the total instrumental delivery rate to be approximately doubled for patients receiving epidural analgesia (relative risk, 2.08 [1.48–2.93]).[13] The broad confidence interval is indicative of the wide variation among studies resulting from variations in practice style and preferences among obstetricians. Furthermore,

sometimes obstetricians in teaching hospitals are more likely to use forceps in women with epidural analgesia. Studies specifically examining use of forceps for dystocia (dysfunctional labor) found no difference between epidural and non-epidural groups (relative risk, 1.53 [0.29–8.08], NS).[13]

The mechanisms by which epidural analgesia could increase instrumental delivery include altered perineal sensation or motor tone, causing a reduction in the urge or ability to push, changes in pelvic muscle tone affecting rotation and descent of the baby, and alteration of endogenous oxytocin release in response to perineal and vaginal stretching (Ferguson reflex). The effect of epidural analgesia may be minimized by reducing the concentration of local anesthetic employed, by the addition of opioids to the mixture, by allowing women to delay the initiation of expulsive efforts after attaining full cervical dilation, and by avoiding specific time limits for the second stage. An older obstetric practice of discontinuing epidural analgesia during the second stage leads to worsened pain scores and no change in forceps delivery, and is therefore no longer recommended.[14,15]

Cesarean Delivery

Retrospective comparisons consistently show a higher rate of cesarean delivery in women who choose epidural analgesia compared to those who do not. However, as noted above, many risk factors for cesarean delivery are more common in women electing epidural analgesia. *Randomized trials consistently show no difference in the rate of cesarean delivery between women in epidural and non-epidural groups.* Meta-analysis of 20 randomized trials including nearly 7,000 patients found no difference in overall cesarean delivery (relative risk 1.07 [0.93–1.23], NS) or in cesarean delivery for dystocia (relative risk 0.90 [0.73–1.12], NS).[12] In addition, several studies have examined the effect of rapidly introducing epidural analgesia to a hospital in which it was previously unavailable. In all such "natural experiment" or sentinel event studies, the rate of cesarean delivery did not change.[16]

Patient Satisfaction and Neonatal Outcome

Patient satisfaction and neonatal outcome are better after epidural than systemic methods of providing childbirth pain relief. Meta-analysis of randomized trials has shown that pain was much worse and dissatisfaction was much more common in the opioid groups, and low 1-min and 5-min Apgar scores, low umbilical cord pH, and the need for nalaxone treatment all were much more common among neonates born to mothers receiving opioid analgesia.[13]

Effect of Epidural Analgesia on Maternal Temperature and the Newborn

Women receiving labor epidural analgesia experience a greater incidence of clinical fever. Previously, observational studies demonstrated a gradual rise in temperature in women receiving epidurals compared to those receiving no analgesia or systemic opioids alone.[17,18] The phenomenon was originally attributed to altered thermoregulation, such as increased heat production due to shivering or decreased heat dissipation due to reduced maternal sweating and hyperventilation. However, it is now evident that this represents an artifact from averaging afebrile women's temperatures and those developing clinical fever.[19,20] Substantial evidence suggests that true clinical fever develops more often in women with epidurals than in those without them. The data come from retrospective observations (which attempt to statistically control for confounding factors such as longer labors, prolonged rupture of membranes, and number of cervical examinations), sentinel event studies (in which epidural analgesia suddenly becomes available to a population), and randomized controlled trials.[21–23]

Epidural-associated fever may have significant effects on the fetus and newborn. An important effect is an indirect influence on the practice of neonatologists. Lieberman[22] demonstrated that babies born to mothers with epidurals underwent evaluation for sepsis four times more often than babies born to mothers electing natural childbirth or systemic opioids. Actual sepsis was vanishingly rare and did not differ between epidural and non-epidural groups. However, other institutions have

not replicated this result, so it may depend on neonatology practice style.[24] Other adverse effects related to intrapartum maternal fever include increased need for bag-mask ventilation and increased incidence of otherwise unexplained neonatal seizures.[25]

A far more worrisome possibility is that maternal fever may cause neonatal brain injury. An association between cerebral palsy and maternal fever was first noted in the 1950s, but the observation was not investigated further until recently. Substantial epidemiologic evidence now confirms a 4–9-fold increase in the risk of otherwise unexplained cerebral palsy in term and near-term infants exposed to maternal fever or clinical or pathologically diagnosed chorioamnionitis.[26,27] Other neonatal brain injuries have also been associated with maternal fever, including neonatal encephalopathy[28] and cognitive deficits at age 9, as measured by the Kaufman Assessment Battery for Children.[29]

The link between maternal fever and neurologic injury in the newborn is most likely inflammation. In experimental pregnant animal preparations, bacterial intrauterine infection causes white matter lesions in the fetuses.[30] In humans, Yoon[31] documented increased IL-6 and IL-8 (pro-inflammatory cytokines) in amniotic fluid in a cohort of pregnancies resulting in babies with cerebral palsy, compared to controls with normal brain development. Moreover, high-dose prednisolone given to the mother blocks epidural-associated fever, though at the cost of increasing neonatal bacteremia.[32]

There is considerable controversy and need for further investigation of this phenomenon. The unanswered questions include:

1. What is the mechanism of epidural-associated fever? In particular, what explains the increased incidence in randomized trials?
2. Does fever itself cause brain injury, or does inflammation cause both fever and injury? The answer is important in deciding how to address the fever.
3. Does epidural-associated fever in the absence of obvious infection cause brain injury?
4. Can epidural-associated fever be safely blocked?

Epidural Analgesia and Breastfeeding

The lactation support and lay birth coaching (doula) communities have long contended that epidural analgesia is a cause of reduced breastfeeding success.[33] Unfortunately, many retrospective comparisons of women who deliver with and without epidural analgesia with regard to breastfeeding are likely confounded by such factors as obstetrical interventions, mode of delivery, systemic medications, and the demographics of mothers selecting epidural analgesia.[34] For example, a 2006 report in an online lactation journal suggested that intrapartum epidural analgesia was strongly negatively correlated with breastfeeding success.[35] The study was plagued with fatal methodological flaws, the greatest of which were that delivery mode was uncontrolled, and that all women self-reporting their analgesic choice as "epidural" also received parenteral meperidine and possibly nitrous oxide.[36]

The effect of epidural analgesia on breastfeeding remains controversial. The best data would be results from RCTs in which women were randomized to epidural vs. alternative analgesia. This has been accomplished more than a dozen times in the last 15 years, but none of these investigations has examined breastfeeding success.[21] Large carefully performed retrospective studies do not show any adverse effect of epidural analgesia.[37–39] Conversely, it appears that systemic opioids, or larger doses of epidural fentanyl, can interfere with early breastfeeding success.[40,41] Nearly all investigators agree that emotional and professional lactation support are the most important factors predicting long-term breastfeeding success.

Summary

Epidural analgesia remains the best choice for most women seeking pain relief in labor. However, even properly conducted epidural analgesia can potentially have adverse effects on the process of labor and delivery and on the condition of the neonate. These effects continue to spark controversy and intense research efforts.

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11
Fetal Monitoring

One of the most important goals for the anesthesiologist caring for a pregnant woman should be to maintain the uteroplacental unit and fetus in optimal condition. Moreover, knowledge of the fetal condition and activity of the uterus can have important implications for the anesthetic plan. Hence, an adequate knowledge of uterine and fetal monitoring is important.

Antepartum Monitoring

Assessment of the fetal condition prior to the onset of labor may affect the timing and mode of delivery.

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Biophysical Profile

Antepartum evaluation of the high-risk fetus is possible by evaluation of five biophysical activities, most of which are assessed by ultrasound:

1. Fetal movement (three gross body or limb movements in 30 min)
2. Fetal tone (at least one extension of an extremity and return to flexion)
3. Fetal breathing movements (at least one episode 30 s in 30 min)
4. Heart rate activity (a nonstress test, see below)
5. Volume of amniotic fluid (at least 2 cm pocket of fluid observable)

The first four parameters reflect the presence of normal fetal central nervous system activity, whereas amniotic fluid volume is an indicator of long-term or chronic fetal condition. These parameters are all measured by ultrasound except for the fetal heart rate. The variables are scored 2 if normal and 0 if abnormal. A score of 8 or 10 is normal, and strongly predicts a healthy newborn with a false-negative rate of less than 0.1%[1] A score of 0, conversely, is strongly correlated with fetal death or neonatal morbidity, and is considered an obstetric emergency.[2] Intermediate scores have equivocal predictive ability, although a score of 4 or below is considered abnormal and is often treated as indication for delivery.

Nonstress Test (NST)

This involves the detection of changes in the fetal heart rate and fetal movement in association with uterine contraction. The fetal heart rate is monitored by Doppler for 20 min (the test can be extended for additional 20 min periods if the fetus is in a sleep cycle). The test is described as reactive (normal) if there are two fetal movements in 20 min with accelerations of the fetal heart rate of at least 15 BPM for at least 15 s. The test is described as nonreactive in the absence of fetal movement or accelerations of the fetal heart rate. Early gestational age, fetal sleep, and maternal smoking can cause a nonreactive test in otherwise normal fetuses. However, a reactive NST is reassuring: stillbirth within one week of a normal test was seen

in only 0.2% of cases in a large observational study.[3] On the other hand, the stillbirth rate after a nonreactive test was just 2.6%, indicating a very high false-positive rate.

Contraction Stress (Oxytocin Challenge) Test

In the presence of a nonreactive NST or other concern for fetal well-being, the contraction stress test (CST), sometimes called the oxytocin challenge test (OCT) may be employed. Intravenous oxytocin is infused to induce three adequate uterine contractions within a 10-min period. *The oxytocin challenge test is contraindicated if there is history of classical cesarean section, placenta previa, high risk of premature labor, or preterm premature rupture of membranes*. The oxytocin challenge test is considered to be positive (nonreassuring) if persistent late decelerations occur in at least 50% of contractions. The test is interpreted as negative (reassuring) in the presence of normal fetal heart rate tracings without late or significant variable decelerations. Other patterns are graded as equivocal or unsatisfactory. Positive tests predict abnormal heart rate patterns in labor and may be an indication for cesarean delivery.

Doppler Velocimetry

Ultrasound examination of blood flow through the umbilical artery towards the placenta can detect conditions of high placental vascular resistance, which correlates with uteroplacental insufficiency and fetal compromise. An elevation in the systolic to diastolic velocity ratio, or detection of absent or reversed diastolic flow, is associated with a higher incidence of perinatal death.[4] Especially in cases of absent or reversed diastolic flow, prompt delivery, usually by cesarean, is indicated unless the fetus is very premature.

Assessment of Fetal Lung Maturity

Tests of amniotic fluid components can be used to assess maturity of the fetal lung sufficient to avoid the neonatal respiratory distress syndrome. Phospholipids, the major components

of lung surfactant, are produced by fetal alveolar cells in a sufficient amount by 36 weeks' gestation but may not be present in sufficient amounts at earlier gestational ages.

Several tests are available. The lecithin/sphingomyelin ratio (L/S) was developed in the 1970 s to predict fetal lung maturity and is normal when the ratio is 2 in uncomplicated pregnancies. For diabetic parturients, the ratio should be at least 3.5 or higher. Measurements of saturated phosphotidylglycerol are occasionally used in normal parturients; the normal value is 500 mg/dL, whereas in diabetics it is 1,000 mg/dL. Both of these classic tests are cumbersome, require a clean, uncontaminated sample of amniotic fluid, and are subject to substantial inter-laboratory variation.

A simpler and faster test relies on the fluorescence generated by polarized light when a specific probe for surfactant is mixed with amniotic fluid. This test, the TD_X-FLM (fetal lung maturity), has become much more popular. It is expressed in milligrams of surfactant per gram of albumin. A FLM value of <40 mg/g indicates immature lung, and above 55 mg/g (60 in some institutions) predicts adequate lung maturity. Intermediate values, unfortunately, are considered indeterminate and have poor predictive ability. Advantages of the FLM are the ability to use a vaginal pool sample in patients with ruptured membranes, its simplicity and rapidity, and its consistency across laboratories. In addition, it has proven reliable at the usual cutoff values in diabetic patients.[5]

Uterine Contraction Monitoring

Assessment of uterine activity is important in predicting the normal progress of labor and also fetal well-being. Parameters describing uterine activity are (1) baseline uterine tone and amplitude, (2) duration of contractions, and (3) the interval between contractions. Normal baseline tone varies between 8 mmHg and 20 mmHg and increases to between 25 mmHg and 75 mmHg during contractions. However, the peak pressure can rise to 130 mmHg with bearing-down efforts in the second stage of labor. A contraction can last from 30 s to 90 s, and the interval between contractions normally varies from 2 min to 3 min.

A tocodynamometer qualitatively measures uterine activity when placed on the skin over the uterus by detecting the ease of indenting the abdominal wall, which decreases during the muscular contraction of the uterus.[6] However, one of the major limitations of external tocodynamometry is inaccuracy from variability in positioning of the instrument, tension of the bands securing it, and distensibility of the abdominal wall. Internal monitoring is more accurate and reliable, as it uses either a fluid-filled catheter in the uterus connected to a pressure transducer, or a direct pressure sensor placed on the end of a probe placed in the uterus. Internal monitoring requires (1) engagement of the presenting part, (2) adequate cervical dilatation, and (3) ruptured membranes. Internal measurement of uterine activity is more commonly used in high-risk cases (e.g., diabetes, postmaturity), when monitoring externally is technically difficult (e.g., morbid obesity), or when quantitative documentation of adequacy of uterine contraction is necessary. Comparative studies, however, have not demonstrated any clinically relevant advantage of internal monitoring.[7]

Fetal Heart Rate Monitoring

The fetal heart rate (FHR) can be monitored by an external probe that uses Doppler ultrasound to detect fetal heartbeats, or by direct application of a bipolar electrode to the fetal presenting part. In either case, the FHR is plotted against time on a strip recorder and inspected for baseline heart rate, variability, and periodic changes, including decelerations and accelerations. The definitions of these terms have recently been reviewed and clarified in an effort to standardize terminology and improve predictive ability of the technique.[8] FHR monitoring is very widely used in US labor units and many other countries worldwide. Remarkably, numerous randomized controlled trials have failed to show significant improvements in fetal condition at birth or a reduction in cerebral palsy or perinatal death.[9]

Baseline Heart Rate

The normal baseline fetal heart rate varies between 110 and 160 beats per minute (BPM), and it is modulated by parasympathetic and sympathetic nerve activity (Fig. 11-1). The

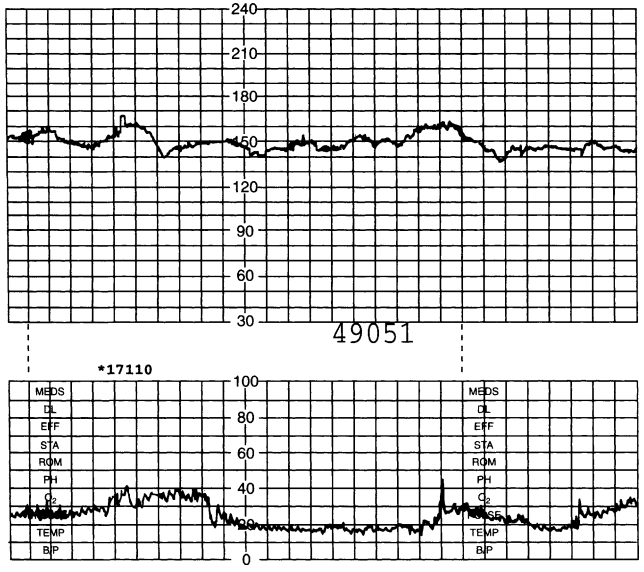

Figure 11–1. Normal fetal heart rate pattern.

baseline is determined by inspection and should not include periodic changes (accelerations and decelerations).

Fetal tachycardia is diagnosed when the baseline exceeds160 BPM.[8] The major causes include:

1. Fetal hypoxia
2. Maternal fever, most often associated with infection
3. Maternal administration of sympathomimetic drugs, e.g., ephedrine, β-mimetic drugs for tocolysis (terbutaline), epinephrine
4. Maternal administration of parasympatholytic drugs, e.g., atropine, phenothiazines
5. Maternal hyperthyroidism
6. Fetal anemia
7. Fetal tachydysrhythmias

Fetal bradycardia is defined as a fetal heart rate less than 110 BPM.[8] The major causes include:

1. Prolonged fetal hypoxia
2. Fetal head or umbilical cord compression

3. Maternal administration of parasympathomimetic drugs, e.g., neostigmine
4. Maternal administration of β-adrenergic antagonists, e.g., propranolol
5. Fetal congenital heart block
6. Combined spinal epidural technique
7. Prolonged maternal hypotension

Baseline Variability

Baseline variability is generally recognized as the single most important parameter for the recognition of intrauterine fetal well-being. Baseline variability is due to a constant battle between the fetal sympathetic (increasing the heart rate) and parasympathetic (decreasing the heart rate) systems. The presence of good baseline variability is an indicator of intact central nervous system as well as normal cardiac functions.

Variability was *previously* classified into short-term variability, representing beat-to-beat differences of 5–15 beats, and long-term variability, fluctuations with a frequency of 3–5 cycles per minute. *This nomenclature is no longer considered valid.* Variability is now classified as absent, minimal (less than 5 BPM), moderate (6–25 BPM), and marked (>25 BPM).[8] Minimal or absent variability (Fig. 11-2) is a strong predictor of neonatal acidosis[10] but there are other causes of diminished variability so the false-positive rate is high. Various factors that can affect variability include:

1. Fetal hypoxemia
2. Maternally administered opioids
3. Maternally administered sedatives and hypnotics, e.g., barbiturates, benzodiazepines, phenothiazines
4. Maternally administered parasympatholytic drugs, e.g., atropine or phenothiazines
5. Fetal sleep
6. Inhalation general anesthesia[11]
7. Extreme prematurity
8. Fetal tachycardia, fetal heart block
9. Maternally administered magnesium sulfate
10. Maternal sepsis

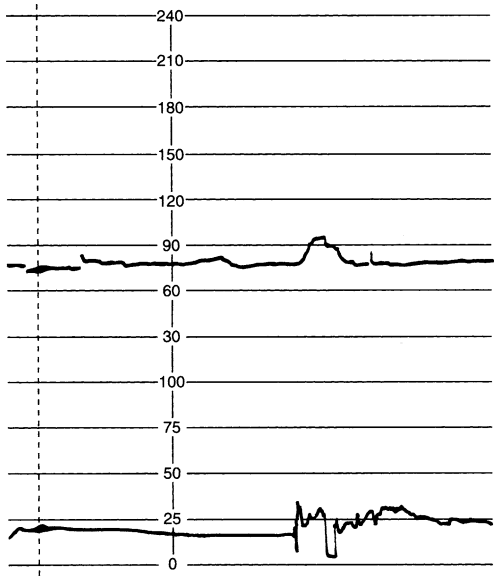

Figure 11–2. Decreased variability of the fetal heart rate.

Fetal Heart Rate Pattern (Periodic Changes)

Periodic changes are defined as transient accelerations or decelerations of the fetal heart rate of short duration followed by a return to baseline levels. Recurrent decelerations accompany more than half of uterine contractions; intermittent changes occur in less than half.[8] There are three categories of decelerations: early, variable, and late.

Early Decelerations

Characteristics of early decelerations (Fig. 11-3) are as follows:

1. Symmetrical, U-shaped deceleration
2. Gradual onset and slow return to baseline (>30 s onset to nadir of FHR)

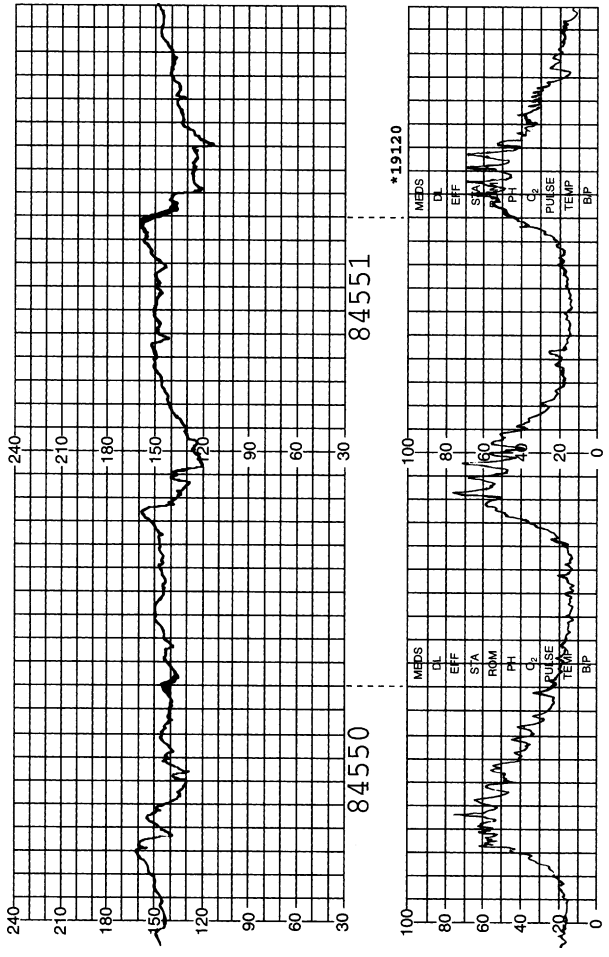

Figure 11–3. Early decelerations.

3. Mirror image of uterine contraction in duration and timing of peak change in HR with peak of contraction corresponding to nadir of FHR
4. Decrease in HR generally not more than 20–30 BPM

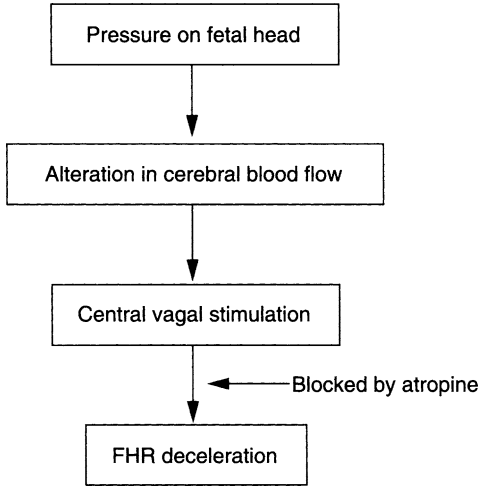

Figure 11–4. Mechanism of early decelerations (FHR = fetal heart rate). (Adapted from Freeman.[17])

Two mechanisms for early deceleration that have been suggested are (1) fetal head compression with increased intracranial pressure (Fig. 11-4) and (2) increased volume of blood entering the fetal circulation during contractions, thus triggering baroreceptor reflex activity. Both of these mechanisms are vagally mediated and can be prevented by atropine.[12]

Variable Decelerations

This is the most common of all fetal heart rate patterns (Fig. 11-5), and the characteristics of this pattern are as follows:[8]

1. Abrupt onset and return to baseline (<30 s)
2. Decrease ≥15 BPM, duration ≥15 s, duration <2 min
3. Variability in duration, shape, size, and timing relative to successive contractions
4. May be accompanied by brief accelerations ("shoulders") before and after departure from baseline

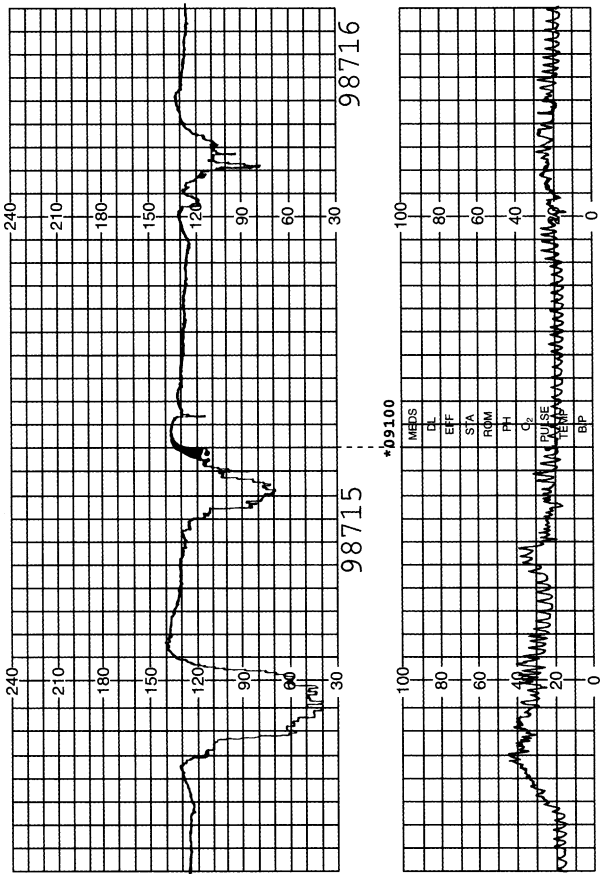

Figure 11–5. Variable decelerations.

Variable decelerations are usually caused by compression of the umbilical cord against fetal body parts, (e.g., head, neck, or shoulder). Because the maximum pressure on the cord is generated at the time of uterine contractions, the deceleration coincides with uterine contraction, but due to changes in relative fetal and cord position they vary in morphology.

They are likely mediated by vagal output. Depending upon the magnitude of the decrease in the fetal heart rate, variable decelerations have been further subdivided into (1) mild (duration less than 30 s and deceleration not below 80 BPM), (2) moderate (regardless of the duration, the fetal heart rate is less than 80 BPM), and (3) severe (duration greater than 60 s and a fetal heart rate less than 70 BPM). However, these classifications have not been tested for predictive validity.[8]

Late Decelerations

Late decelerations (Fig. 11-6) are characterized by the following:

1. Symmetrical gradual onset and return to baseline (≥30 s from onset to nadir).
2. Onset and nadir lag beginning and peak of uterine contraction (typically ≥30 s)
3. Return to baseline after the end of the associated uterine contraction
4. Decrease in FHR is usually mild (10–20 BPM) and rarely more than 30–40 BPM.

There is some correlation between the frequency of late decelerations and the degree of fetal hypoxia. Moderate variability in the setting of late decelerations is somewhat less concerning than diminished or absent variability with the same decelerations.[8] The major cause of late decelerations is reduced placental perfusion, as can be seen during hypotension (e.g., following regional analgesia), aortocaval compression, placental abruption, maternal diabetes mellitus, preeclampsia, and post-dates pregnancy.

Besides these three main patterns, the other patterns that have been described are prolonged decelerations and a sinusoidal pattern. *Prolonged decelerations* are decreases in HR ≥15 BPM which last ≥2 min but <10 min. Longer decelerations are considered baseline changes. Prolonged decelerations are considered concerning but not as ominous as recurrent late or variable decelerations with absent variability. A *sinusoidal pattern* is associated with a sine-wave pattern above and below the baseline with a frequency of 3–5 per min. A benign

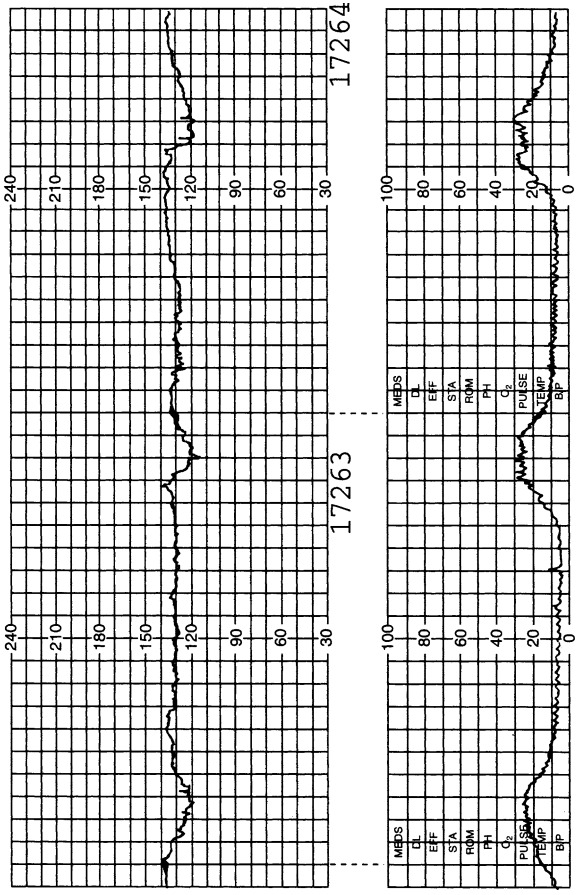

Figure 11–6. Late decelerations. (Adapted from Martin.[18])

sinusoidal pattern has been associated with opioid agonist–antagonist drugs (e.g., butorphanol). A major obstetric cause is severe fetal anemia usually associated with Rh incompatibility. In this setting, the sinusoidal pattern is considered ominous.[8]

Other Modalities

Fetal Scalp Blood Sampling

Fetal scalp blood pH determination is a direct way to test for the presence of acidemia. A sample of capillary blood is obtained by a small incision in the fetal scalp and analyzed for pH, typically in duplicate or triplicate. Normal fetal scalp pH varies between 7.25 and 7.32; mild acidemia is documented when the pH varies between 7.20 and 7.24; and severe acidemia is noted when the pH is less than 7.20. Unfortunately, the sensitivity and specificity of the test in predicting umbilical blood pH at delivery is modest.[13] Furthermore, scalp blood pH laboratories are expensive and volume is not generally high enough to justify the cost for the vast majority of labor units. Thus the popularity of the technique has sharply declined over the last decade.[14]

Fetal Pulse Oximetry

In theory, continuous measurement of fetal oxygenation should provide minute-by-minute information of fetal well being, because ultimately poor oxygenation is the cause of most fetal compromise during labor. A modified pulse oximeter uses a reflectance probe, generally placed alongside the fetal cheek or temple. Unfortunately, the technique has not proven to reduce interventions for presumed fetal compromise, including cesarean delivery, nor has its use improved fetal condition at birth.[15] ACOG does not endorse its use at this time.[16]

Implications for Anesthesia Care

The anesthesiologist should be aware of fetal assessment for several reasons. First, the timing and urgency of delivery are often dictated by the results of fetal monitoring. Awareness of a deteriorating FHR pattern or poor biophysical profile can alert the anesthesiologist to prepare for urgent delivery, or to encourage a parturient and the obstetric caregivers to initiate regional anesthesia in anticipation of emergency delivery.

Second, decelerations and other nonreassuring FHR tracings may require obstetrical interventions for ultimate resolution but the anesthesiologist may be called on to seek and remedy reversible causes. This may include proper positioning to avoid aortocaval compression, use of supplemental oxygen, correction of hypotension, intravenous fluid bolus, and rarely maneuvers to reduce uterine tone (e.g., intravenous nitroglycerin). Finally, enhanced communication between the obstetrical, nursing, and anesthesiology providers is facilitated by a common understanding of the factors influencing the formation of the obstetrical care plan.

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12
Anesthesia for Cesarean Delivery

S. Datta et al., *Obstetric Anesthesia Handbook*,
DOI 10.1007/978-0-387-88602-2_12,

In recent years, the frequency of cesarean delivery has increased markedly. In 1965, the incidence was 4.5%.[1] Since then there has been a steady increase in cesarean delivery rate driven by both an increase in the percentage of all women having a first cesarean and a decline in the percentage of women delivering vaginally after a previous cesarean. As per Center for Disease Control, Atlanta, USA, the cesarean delivery rate in USA in 2005 was 30.2%. The rate of cesarean delivery varies across the world with England, 23% in 2004, Brazil 47% (some health districts with 85%), and India (Delhi 19–35%). In Sweden, Denmark, and Netherlands, the cesarean delivery rate is still close to 10% with some of the world's lowest maternal and perinatal mortality rates.[2–4]

Successful anesthesia for cesarean delivery can be accomplished in a number of ways. Common to all is the need for expert technical skills and understanding of maternal and fetal physiology, pathophysiology of associated diseases, and pharmacology. The two major anesthetic approaches are regional and general anesthesia. Discussion of regional anesthesia will include three techniques – spinal, epidural, and combined spinal epidural anesthesia – since local infiltration and field blocks are rarely used in the United States.

Regional Anesthesia

Spinal Anesthesia (Subarachnoid Block)

The advantages of spinal anesthesia for cesarean delivery are as follows:

1. Simplicity of technique
2. Speed of induction (in contrast to an epidural block)
3. Reliability
4. Minimal fetal exposure to the drug(s)

5. An awake parturient
6. Minimization of the hazards of aspiration

Disadvantages of spinal anesthesia for cesarean delivery include the following:

1. High incidence of hypotension
2. Intrapartum nausea and vomiting
3. Possibility of headaches after dural puncture
4. Limited duration of action (unless a continuous technique is used)

Problems Associated with Spinal Anesthesia

Hypotension. Following induction of spinal anesthesia for cesarean delivery, the incidence of maternal hypotension, usually defined as a decrease in systolic blood pressure to below 100 mmHg or a decrease of more than 30 mmHg from the preanesthetic value, can be as high as 80%. These hemodynamic changes result from a blockade of sympathetic vasomotor activity that is accentuated by compression of the aorta and inferior vena cava by the gravid uterus when the patient is in the supine position.

The higher the segmental sympathetic blockade (especially greater than T4), the greater the risk of hypotension and associated emetic symptoms.[5] The supine position significantly increases the incidence of hypotension. Ueland and colleagues observed an average decrease in blood pressure from 124/72 mmHg to 67/38 mmHg in mothers who were placed in the supine position following the induction of spinal anesthesia, whereas the blood pressure averaged 100/60 mmHg for mothers in the lateral position (Fig. 12-1).[6]

The significance of maternal hypotension lies in the threat to the well-being of both mother and fetus if the decreases in the blood pressure and cardiac output are not promptly recognized and corrected. Brief episodes of maternal hypotension can lower Apgar scores, prolong the time to sustained respiration, and produce fetal acidosis.[7,8] Short periods of hypotension (not more than 2 min) result in minimal fetal acidosis but no effect on newborn neurobehavioral findings between 2 h and 4 h of age. With prolonged periods of hypotension Hollmen and associates have shown neurological changes for at least

48 h in infants born to mothers who had epidural anesthesia for cesarean delivery.[9] Since spinal anesthesia offers major clinical advantages for cesarean delivery, efforts have been directed at preventing maternal hypotension. Prehydration or acute volume expansion (15–30 min prior to cesarean delivery) with 1,000–1,500 mL of lactated Ringer's solution has been suggested.[10] This dictum was challenged and a group from South Africa found no beneficial effect of a predetermined amount of volume expansion before the induction of spinal anesthesia for cesarean section.[11] In a double-blind study, Park et al.[12] randomized 55 parturients randomized to receive one of 10 mL/kg, 20 mL/kg, or 30 mL/kg of crystalloid volumes prior to induction of spinal anesthesia. Measurements included mean arterial blood pressure (MAP), cardiac index (CI), and systemic vascular resistance index (SVRI) recorded using noninvasive thoracic impedance monitoring until delivery. Maternal and neonatal colloid oncotic pressures were measured. All groups showed declines in MAP and SVRI from baseline at 5 min after spinal anesthesia, but the amount of decline did not differ among groups. Total ephedrine and additional intravenous (i.v.) fluid administered did not differ among groups.

Similar findings were also observed by Jackson et al.[13] Hence a predetermined amount of volume expansion may not be necessary before initiation of spinal block for cesarean section. On the other hand, colloid administration (1,000 ml Dextran 60, 500 ml Hydroxyethyl Starch 10%) prior to initiation of spinal anesthesia has a protective effect in minimizing the degree of hypotension.[14,15]

Several authors have observed fetal hyperglycemia, acidosis, and, ultimately, neonatal hypoglycemia when a dextrose-containing solution was used for acute volume expansion.[16,17] This has led to not recommending the use of dextrose-containing solutions for cesarean delivery unless there is an indication.

Vasopressors. The value of the administration of a prophylactic vasopressor is still controversial. From a systematic meta-analysis review of available studies to determine the dose–response characteristics of prophylactic i.v. ephedrine for the prevention of hypotension during spinal anesthesia for cesarean delivery, the authors concluded that the efficacy is

poor at smaller doses, whereas at larger doses the likelihood of causing hypertension is actually more than that of preventing hypotension.[18] On the contrary, phenylephrine (10 μgm/min) added to prophylactic ephedrine infusion (2 mg/min) halved the incidence of hypotension following the induction of spinal anesthesia as compared to ephedrine-alone group.[19] The authors do not routinely use prophylactic ephedrine because it might not be necessary in all cases and hypertension can develop in some cases. However, if there is a trend towards decreasing blood pressure, prophylactic ephedrine is used by some anesthesiologists to decrease chances of further hypotension. There is general agreement that if hypotension should develop, it should be promptly treated by a combination of a bolus infusion of intravenous crystalloid, further uterine displacement if possible, and the administration of intravenous doses of ephedrine, beginning with 5–10-mg increments to normalize the blood pressure. Although ephedrine has been the drug of choice to treat hypotension for decades in this institution, recent literature favors the rejuvenation of the use of phenylephrine to treat hypotension following spinal anesthesia

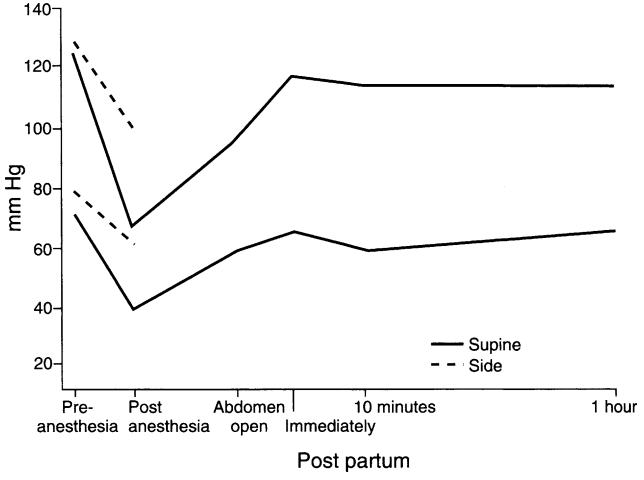

Figure 12–1. Effect of maternal blood pressure during cesarean section under spinal anesthesia. (Adapted from Ueland et al.[6])

induction. This has changed practice among some anesthesiologists. The studies claiming superiority of phenylephrine over ephedrine state the following advantages: higher mean umbilical artery pH, less nausea and vomiting, and avoidance of excessive tachycardia.[20,21] However, a recent study found no significant difference among these factors between the phenylephrine and ephedrine group even in nonelective cesarean deliveries.[22] Furthermore, no differences were found in the incidence of hypotension when a combination of phenylephrine and ephedrine was used versus using either one of them alone.[21,23]

In conclusion, there is a choice of vasopressors that can be used. It does not matter what is used as long as the hypotension is corrected. However, in some situations, tachycardia followed by ephedrine administration may be contraindicated (cardiac problems) and under these circumstances phenylephrine is a good alternative choice. A final controversy yet to be addressed is how phenylephrine affects the uteroplacental blood flow when there is a prior uteroplacental insufficiency.

The incidence of hypotension during spinal anesthesia for cesarean delivery in parturients who have active labor is lower than in pregnant women not in labor.[24] Possible explanations may be (1) the *autotransfusion of approximately 300 mL of blood into the maternal systemic circulation with intermittent uterine contractions,* (2) *a decrease in the size of the uterus secondary to a loss of amniotic fluid if the membranes are ruptured,* and (3) *higher maternal catecholamine concentrations in parturients in labor.*

Nausea and Vomiting. These symptoms commonly accompany spinal anesthesia. The mechanism is unclear but probably involves (1) systemic hypotension, which decreases cerebral blood flow and produces cerebral hypoxia, and (2) traction on the peritoneum or other viscera, which produces a vagal response manifested by a decrease in the heart rate and a resultant decrease in cardiac output. Datta et al. have evaluated the effectiveness of prompt treatment of any decrease in blood pressure on the prevention of nausea and vomiting. Their conclusion was that intravenous ephedrine, when given as soon as any reduction in blood pressure is detected, prevents a further decrease in blood pressure and significantly

diminishes the incidence of nausea and vomiting. In addition, acid–base values from the umbilical vessels of newborns whose mothers were so treated were significantly better than in the newborns of mothers who developed frank hypotension.[25] As stated in the foregoing paragraphs, in one study authors observed a reduction of nausea and vomiting when phenylephrine was used in comparison to ephedrine to treat maternal hypotension.[21]

Traction of the uterus and/or peritoneum at the time of surgery may increase the incidence of emetic symptoms in the presence of inadequate regional anesthesia.[26] Visceral pain from traction of the peritoneum or abdominal viscera (e.g., exteriorization of the uterus or stretching of the lower uterine segment) will transmit afferent stimuli via the vagus nerve to stimulate the central vomiting center. Adequate sensory anesthesia can be obtained with appropriate doses of local anesthetic, and this will also decrease the incidence of discomfort in parturients. The addition of intrathecal or epidural opioids will intensify the quality of sensory anesthesia and will decrease the incidence of intraoperative nausea and vomiting.[27,28] Nausea and vomiting following delivery of the baby can be minimized with the administration of small doses of intravenous droperidol, metoclopramide, ondansetron, dexamethasone, and combination of droperidol and dexamethasone (Figs. 12-2 and 12-3).[29–33] In United States, droperidol is not being used for this purpose because of FDA directive (prolonged QT interval and torsades de pointe).

Scopolamine patch has also been shown to be effective in decreasing nausea and vomiting.[34] In addition, acupressure via wrist band for P6 point has been shown to be somewhat effective in decreasing nausea and vomiting during cesarean delivery.[35,36] Ephedrine 25–50 mg i.m. has been used for nausea and vomiting in nonpregnant patients and is also an option during cesarean delivery. The beneficial effect of ephedrine is due to sympathomimetic effect of ephedrine on vestibular apparatus as well as improving medullary blood flow to chemoreceptor triggering zone.[37] Some anesthesiologists observed the benefit of having patients smell isopropyl alcohol in the treatment of nausea and vomiting. Lastly, subhypnotic doses of either midazolam (1 mg bolus, 1 mg/h infusion)

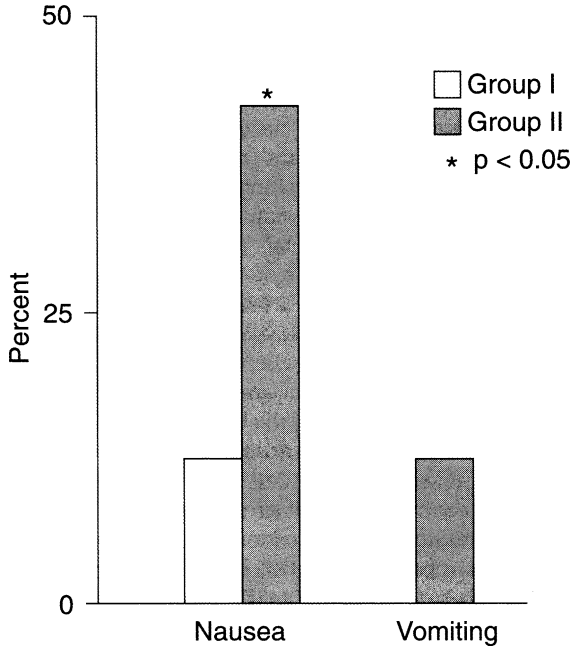

Figure 12–2. Incidence of nausea and vomiting with intravenous droperidol following delivery of the fetus during cesarean section (group 1-droperidol, group 2-saline).[29]

or propofol 20 mg bolus, 1 mg/kg infusion have also been effective in decreasing nausea and vomiting during cesarean delivery under spinal anesthesia.[38]

Headache. Headache as a result of dural puncture (PDPH) is the most troublesome complication of spinal anesthesia in obstetrics. The reported incidence of PDPH varies greatly from institution to institution (0–10%). Over the years several interesting techniques have been reported to decrease the incidence of PDPH: (1) the method of insertion of the spinal needle may be an important factor in reducing PDPH. A recent meta-analysis by Richman et al. showed a significant reduction in PDPH with parallel insertion of the spinal needle in relation to the dural fibers.[39] (2) Needles of different sizes were tried

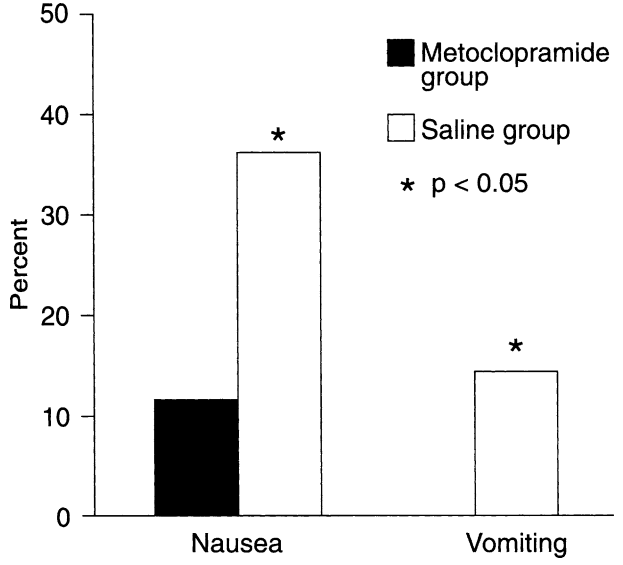

Figure 12–3. Incidence of nausea and vomiting with intravenous metoclopramide following delivery of the fetus during cesarean section. (Adapted from Chestnut.[31])

to observe the incidence of PDPH.[40] When 27-gauge Quincke needles were used, the incidence of PDPH in the author's institution remained 2–3%. (3) Configuration of the needles is also important. The long-beveled Quincke needle is associated with a higher incidence of headache than are pencil-point needles like the Greene, Whitacre, and Sprotte (Fig. 12-4).[41] This might be related to the amount of injury to the dural fibers. A meta-analysis also supports that noncutting smaller-size needles are associated with decreased PDPH.[42]

Ready and colleagues observed the effect of needle size and angle of dural puncture in relation to the rate of transdural fluid leak.[43] Quincke needles with a 30-degree approach caused a rate of leak across the dura significantly less than those following 60- and 90-degree approaches. An approach perpendicular to the dural fibers was associated with a higher incidence of PDPH. The 22-gauge Whitacre needle was also

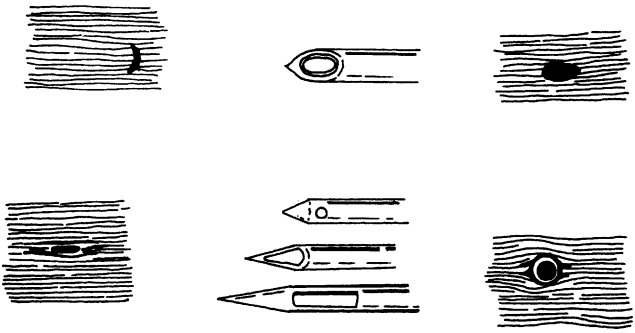

Figure 12–4. Openings made in the dura during and after insertion of pencil-point needles (Pajunk, Greene, Whitacre) and beveled needle (Quincke). Small openings are made by pencil-point needles.

associated with less leak than the 22-gauge Quincke needle. When a 25-gauge Whitacre needle was used, the incidence of headache in the author's institution was about 1%. The majorities of headaches are mild and self-limited and resolve without problems. Oral and intravenous caffeine can decrease the incidence of headaches temporarily.[40]

Technical Factors. A sensory level between the fourth and sixth thoracic dermatome is necessary for adequate anesthesia. This level is achieved in the pregnant women with doses of local anesthetic well below the required amounts in nonpregnant individuals in both spinal and epidural anesthesia (Fig. 12-5). A hyperbaric solution is preferred for cesarean section because it tends to spread to the thoracic kyphosis at approximately T5–6[44] regardless of the parturients height. Norris observed no correlation between the height or weight of parturients and the spread of spinal anesthesia when using a fixed dose (12 mg) of 0.75% hyperbaric bupivacaine in women between 4′11″ and 5′8″.[45] DeSimone and colleagues, on the other hand, compared a 12-mg with a 15-mg dose of hyperbaric bupivacaine for cesarean section and observed a significantly higher spread with 15 mg.[46] Hartwell et al. studied the correlation between vertebral length measured from

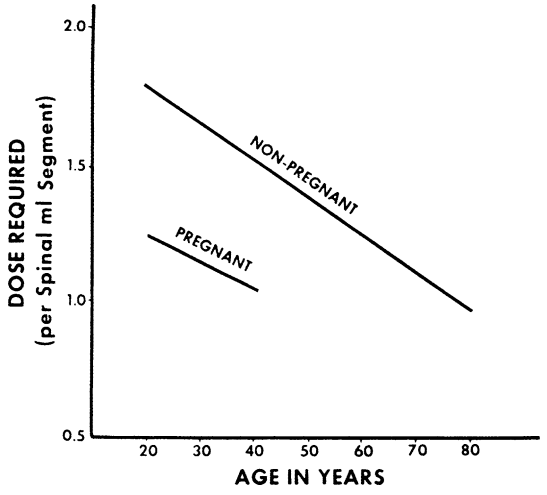

Figure 12–5. Dose required (milliliters of lidocaine per spinal segment) in parturients and nonpregnant patients. (From Bromage, p. 566.[148] Used with permission from Elsevier.)

C7 to the level of the iliac crest and to the sacral hiatus and the sensory anesthetic level after the subarachnoid administration of 12 mg of hyperbaric bupivacaine for cesarean section. There was no correlation between patient height, weight, or body mass index and the sensory anesthesia level; however, interestingly, there was a correlation between vertebral length and sensory anesthesia level.[47] Twelve milligrams should be adequate for the majority of parturients.

Sprague showed that in order to avoid placing the patient in the supine position for even spread of the local anesthetic, spinal anesthesia should be induced with the patient in the *right* lateral position. Subsequent placement in the left semilateral position with a wedge under the right hip allows for immediate left uterine displacement and for more even distribution of the hyperbaric local anesthetic through the subarachnoid space.[48]

Medications for Spinal Anesthesia

Table 12-1lists current medications as well as their durations of action.

Table 12–1. Medications for Spinal Anesthesia

Drugs in Current Use	Duration of Surgical Anesthesia
0.5% tetracaine in 5% dextrose	90–120 min
5% lidocaine in 7.5% dextrose in water	45–60 min
0.75% bupivacaine in 8.5% dextrose in water	90–120 min
0.5% bupivacaine in 8.0% dextrose in water	90–120 min but not yet approved by FDA
5% meperidine in 10% dextrose, same volume to make it hyperbaric	45–50 min

Hyperbaric bupivacaine, 0.75%, has become a popular local anesthetic for cesarean section in our hospital (Brigham and Women's). The addition of 0.2 mg of epinephrine will improve the quality of analgesia.[49,50] Sensory and motor block is prolonged by about 30 min. [49,50] However, the onset of sensory block to T4 is delayed by about 2–6.5 min.[51] Intrathecal narcotics have been administered together with local anesthetics at the time of administration of spinal anesthesia. A combination of local anesthetic and narcotic has been shown to intensify the sensory anesthesia; visceral nociceptive afferents have also been found to be blunted. Fentanyl (6.25–12.5 μg) mixed with 0.75% bupivacaine is associated with excellent intraoperative analgesia as well as a few hours of postoperative pain relief.[27] Courtney and colleagues observed longer postoperative pain relief with 10 μg of sufentanil as compared with 6.25 μg of fentanyl.[52]

Subarachnoid morphine, 0.1–0.5 mg, mixed with 0.75% hyperbaric bupivacaine has also been used,[53] with postoperative pain relief lasting between 17 h and 27 h. However, one should be aware of the possibility of delayed respiratory depression with the use of subarachnoid morphine. Addition

of small doses of clonidine (30–60 μg) mixed with fentanyl and morphine will improve postoperative pain relief. Using the dose–response effect of intrathecal morphine, 0.1 mg was observed to be optimal with fewer side effects.[54] Butorphanol 0.4 mg mixed with 0.75% hyperbaric bupivacaine has been used in the subarachnoid space. Postoperative analgesia lasted as long as 8.2 h, but this has not become popular at this time.[55]

Interestingly, intrathecal meperidine (1 mg/kg) without local anesthetics has been used for cesarean section with success. One study compared 5% hyperbaric lidocaine to 1 mg/kg hyperbaric meperidine for cesarean section. The duration of sensory anesthesia was longer with hyperbaric meperidine.[56] Meperidine 10 mg added to intrathecal bupivacaine for cesarean section was associated with prolonged postoperative analgesia but with greater intraoperative nausea and vomiting in one study. [57] The newer anesthetics levobupivacaine and ropivacaine do not seem to add any great advantage. One study compared bupivacaine, levobupivacaine, and ropivacaine for cesarean section anesthesia and concluded that the racemic mixture of bupivacaine combined with sufentanil provided significantly superior anesthesia, and remains an appropriate choice when performing cesarean section. [58] The anesthesiologists at Brigham and Women's Hospital use 12–13 mg of hyperbaric 0.75% bupivacaine, 10–20 μg of fentanyl, and 200 μg of preservative-free morphine for spinal anesthesia.

Summary of Spinal Anesthesia for Cesarean Section

1. Bicitra, 30 mL, and metoclopramide, 10 mg, intravenously (unless contraindicated)
2. Good intravenous access and use of Ringer's lactate, unless contraindicated
3. Monitoring of pulse, blood pressure, electrocardiogram (ECG), and oxygen saturation
4. Hyperbaric bupivacaine, 0.75% (12–13 mg), except in extremes of height, mixed with 10–20 μg of fentanyl and 100–200 μg of morphine, depending upon the institution.

At Brigham and Women's, we typically use 200 μg of morphine.
5. Use of 27-gauge Quincke or 25-gauge Whitacre needles
6. Right lateral position for induction of spinal anesthesia
7. Routine left uterine displacement during surgery until delivery of the baby
8. Treatment of decreases in maternal blood pressure with phenylephrine, 40 μg, in incremental doses or ephedrine in 5–10 mg increments.
9. Oxygen by face mask
10. Postoperative monitoring for delayed respiratory depression if subarachnoid morphine is used

Continuous spinal anesthesia can be used in patients with short stature and morbidly obese parturients because one can use small doses to gradually attain a desired level of sensory anesthesia to decrease the incidence of hypotension and avoid an overly high block.

Contraindications for Spinal Anesthesia for Cesarean Section

1. Severe maternal bleeding
2. Severe maternal hypotension
3. Coagulation disorders
4. Some forms of neurological disorders
5. Patient refusal
6. Technical problems
7. Short stature and morbidly obese parturients due to the fear of high spinal block
8. Sepsis, infection in the area of needle insertion or generalized

Continuous spinal anesthesia may be used if there is an accidental dural tap while performing the epidural anesthesia, or where intentional dural puncture is made by an epidural needle, e.g., in obese parturients. Small increments of local anesthetic, 6 mg of bupivacaine mixed 10 μg of fentanyl and 0.2 mg of morphine, can be used for initiation of the block. Further local anesthetic can be given by the catheter if needed.

Epidural Anesthesia

Advantages of epidural anesthesia for cesarean section include the following:

1. Lesser incidence and severity of maternal hypotension
2. Avoidance of dural puncture, which may diminish the incidence of headaches. At this time this is controversial.
3. With a catheter technique, anesthesia can be provided for longer operations. In addition, postoperative pain relief can be also achieved with local anesthetics and epidural narcotics

Disadvantages of epidural analgesia include the following:

1. Increased complexity of the technique with a greater chance of failure. Slower onset of anesthesia, so not useful in urgent situations; however, to certain extent by adding bicarbonate to the local anesthetics and the use 3-chloroprocaine can hasten the onset time.
2. Need for larger amounts of local anesthetic agent

Problems Associated with Epidural Anesthesia

Cardiovascular Effects. There are substantial differences between the cardiovascular effects of lumbar epidural anesthesia and spinal anesthesia for cesarean delivery. A reduction in arterial blood pressure is usually less in epidural anesthesia because of the slower onset of the block. Local anesthetic containing epinephrine (1:200,000), when used for cesarean section, may contain epinephrine from 100 μg to 125 μg when injected into the epidural space. Systemic absorption of epinephrine can cause a decrease in maternal blood pressure because of its β-mimetic effect.[59]

Technical Factors. Maternal position affects both the adequacy of anesthesia and fetal outcome. The investigators at Brigham and Women's Hospital found that placing the mother in the lateral position during induction of a lumbar epidural block for cesarean delivery did not affect the adequacy of the block and resulted in improved acid–base values in umbilical cord blood.[60] Higher concentrations of bupivacaine were found in the umbilical cord blood of the more acidotic fetuses delivered to mothers who had been supine. This is probably

the result of "ion trapping" of the weakly basic local anesthetic in the more highly acidic fetal blood. However, none of the newborns in this study demonstrated any untoward effects as a result of the higher level of bupivacaine. Our practice is to keep parturients in the semi-sitting position during induction of anesthesia. With this technique, one can ensure an adequate block of the sacral nerves in order to block pelvic pain during delivery and during traction of the vagina and peritoneal structures. An additional advantage of this maneuver is the observation that the cardiac output in the pregnant woman is higher in the sitting position as compared with the supine position.

Complications of Epidural Anesthesia

1. Unintentional intravascular injection of local anesthetic through the epidural catheter occurs in approximately 2.3% of patients.
2. The incidence of dural puncture varies between 0.2% and 20%, depending on the experience of the anesthesiologist. The incidence of PDPH with a 17-gauge needle may be as high as 76%.
3. The incidence of shivering after induction of epidural anesthesia has been observed to vary from 14% to 68%. The peak onset of shivering usually takes place 10 min after induction of epidural anesthesia.[61] The mechanism of shivering is not known; however, the incidence can be decreased by epidural fentanyl[62] or sufentanil[63] or by intravenous meperidine.

Contraindications for Epidural Anesthesia

1. Severe maternal hypotension
2. Coagulation disorders
3. Some forms of neurological disorders
4. Patient refusal
5. Technical problems
6. Sepsis, local infection in the area of needle insertion or generalized

Local Anesthetics for Epidural Anesthesia

Table 12-2 lists current medications as well as their durations of action.

Table 12–2. Local Anesthetics for Cesarean Delivery

Drugs in Current Use	Duration of Surgical Anesthesia
Bupivacaine 0.5%	75–90 min
Ropivacaine 0.5%	75–90 min
Levobupivacaine 0.5%	75–90 min
Lidocaine with epinephrine 2%	75–90 min
2-chloroprocaine 3%	25–35 min

Unless contraindicated, 2% lidocaine with epinephrine is our drug of choice because of its excellent sensory and motor anesthesia and its sufficiently long duration of action. The lower concentration of bupivacaine (0.5%) provides a slower onset of action; hence, there is a lesser incidence of hypotension. Both 0.5% ropivacaine and 0.5% levobupivacaine have been compared with 0.5% bupivacaine for cesarean section.[64–66] No significant clinical outcome differences were observed between levobupivacaine and bupivacaine to change our practice.[64] Similarly, no significant differences were found between ropivacaine and bupivacaine, except one study that found prolonged motor block with 0.75% ropivacaine.[65,67,68] The addition of 50–100 μg of fentanyl to local anesthetic agents can improve the intensity of sensory anesthesia[69] and thus can reduce the requirements of added analgesics and tranquilizers during the operation. *2-Chloroprocaine is an ideal local anesthetic in the presence of fetal distress. Its short maternal half-life as well as fetal plasma half-life will be beneficial in such a situation.* The onset of the block can be hastened by adding sodium bicarbonate to the local anesthetic (1 ml to 9–10 ml of local anesthetic). This will not only make the block faster but also improve the quality of the block. One of the disadvantages of chloroprocaine for cesarean section is the poor quality and shorter duration of analgesia when epidural μ-agonist narcotics are used following the use of this local anesthetic. The

mechanism of this is not known at the present time. However, 2-chloroprocaine or its metabolite chloroaminobenzoic acid can act as a μ-antagonist. When the κ-agonist butorphanol, 2 mg, was used epidurally, we observed effective pain relief following the use of 2-chloroprocaine.[70]

Morphine, 3–5 mg, has been used for postoperative pain relief following epidural anesthesia, and its effect can last between 12 h and 24 h.[53] Several anesthesiologists use smaller amounts of epidural morphine (3 mg).[54,64,71] Our practice is to use 3 mg preservative free morphine epidurally for postoperative pain relief.

Summary of Epidural Anesthesia for Cesarean Section

1. Bicitra and metoclopramide, 10 mg intravenously (unless contraindicated)
2. Ringer's lactate intravenous infusion as deemed necessary
3. Monitoring of pulse and blood pressure, ECG, oxygen saturation, and fetal heart rate tracing during induction of anesthesia
4. Two percent lidocaine with epinephrine, 0.5% bupivacaine, 0.5% ropivacaine, 0.5% levobupivacaine, or 3% 2-chloroprocaine. Fractionated doses of local anesthetic agent injected epidurally until T4-level sensory analgesia is achieved. Approximately 20 ml may be required to achieve this level. If prior labor analgesia is being provided via epidural route, surgical level can be obtained with about 15 ml given in fractionated quantities (3–5 ml boluses).
5. Routine left uterine displacement
6. Treatment of decreases in maternal blood pressure with ephedrine (5–10 mg at a time) and volume expansion. Phenylephrine (40 μg) may be used in incremental doses if ephedrine is contraindicated.
7. Oxygen by face mask (6–8 L/min) to maintain better maternal and fetal acid–base values (Fig. 12-6)
8. Postoperative monitoring for delayed respiratory depression if epidural morphine is used

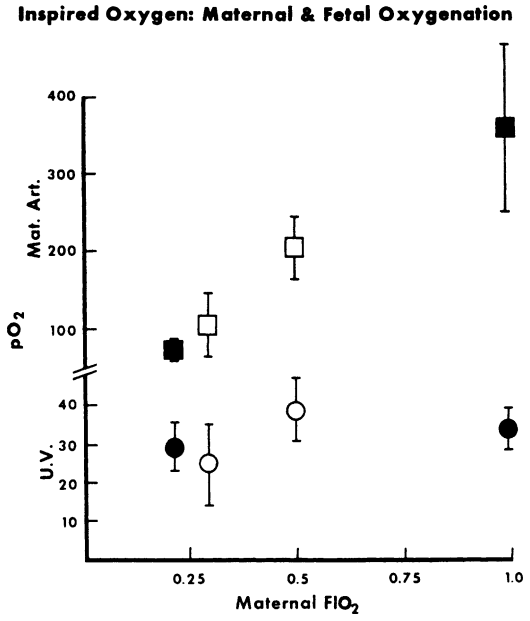

Figure 12–6. Influence of maternal inspired oxygen on maternal and fetal oxygenation at birth during cesarean section under epidural and general anesthesia. *Filled circles* (fetal) and *filled squares* (maternal) indicate epidural analgesia, whereas *open circles* and *squares* indicate a light general anesthesia plus relaxant. (From Bromage, p. 578.[148] Used with permission from Elsevier.)

Cardiovascular Complications of Bupivacaine and Neurological Complications of 2-Chloroprocaine

Albright in a 1979 editorial in *Anesthesiology* pointed out the higher incidence of cardiac arrest associated with highly lipid-soluble and protein-bound drugs like etidocaine and mainly bupivacaine.[72] The incidence of cardiac arrhythmias and cardiac arrest was higher in parturients receiving 0.75%

bupivacaine; in 1980, the FDA banned the use of 0.75% bupivacaine in obstetric patients. Numerous animal studies were performed following Albright's report regarding the central nervous system (CNS) and cardiovascular system toxicity of different clinically used local anesthetics, and these can be summarized as follows:

1. The CC/CNS ratio (CC toxicity, cardiovascular collapse; CNS toxicity, convulsion) was lower for bupivacaine and etidocaine when compared with lidocaine.
2. Ventricular arrhythmias, fatal ventricular fibrillation, and cardiac arrest occurred after the rapid intravenous injection of bupivacaine.
3. *Pregnant animals were found to be more sensitive than nonpregnant animals to the cardiotoxic effects of bupivacaine.*
4. *Cardiac resuscitation following bupivacaine toxicity was much more difficult than in the case of lidocaine*. Hypoxia and acidosis were important factors contributing to this problem.

As a rule, the cardiovascular system is more resistant than the CNS to local anesthetic. The CC/CNS ratio of lidocaine in adult sheep was 7.1 ± 1.1, whereas with bupivacaine and etidocaine it was 3.7 ± 0.5 and 4.4 ± 0.9, respectively.[73–75] The same group of observers also noticed a higher sensitivity of the myocardium to bupivacaine in pregnant animals than in nonpregnant animals. The CC/CNS ratio for nonpregnant animals was 3.7 ± 0.5 as compared with 2.7 ± 0.4 in pregnant animals.[75,76] In a subsequent study, the authors did not observe any enhancement of systemic toxicity of ropivacaine or bupivacaine during pregnancy. The exact mechanism for this difference in sensitivity in pregnant animals is not known; however, the authors speculated that the lower protein binding in pregnancy may be responsible for this increased sensitivity. Using an in vitro model, Moller and colleagues observed a significantly higher depression of V_{max} of ventricular muscles obtained from progesterone-treated animals as compared with controls.[76] It is possible that progesterone and its metabolites can interfere with sodium, potassium, or calcium channels. A study using B-estradiol in a rabbit ventricular muscle and Purkinjee fibers model showed higher

degree of depression of V_{max} with bupivacaine.[77] Clarkson and Hondeghem, observing the sodium channel blocking effect of bupivacaine, suggested that in high concentrations lidocaine blocked sodium channels in a fast-in–fast-out manner, bupivacaine in low concentrations blocked sodium channels in a slow-in–slow-out manner, whereas in high concentrations the block was of the fast-in–slow-out type.[78] The practical implication of this phenomenon is important: this might be one of the reasons for the longer resuscitation time required for bupivacaine cardiotoxicity. Kasten and Martin showed successful cardiovascular resuscitation after a massive intravenous bupivacaine overdosage in dogs by (1) ventilation with 100% O_2, (2) open heart massage, (3) bretylium for ventricular tachycardia; if circulation is present, cardioversion will be also necessary, and (4) epinephrine and atropine for electromechanical dissociation and bradycardia[79] Recently, intravenous lipid emulsion (bolus 1.2–2 ml/kg, infusion 0.25–0.5 ml/kg/min) has been the most favored method of treating bupivacaine and ropivacaine cardiac toxicity. It reverses local anesthetic toxicity by extracting lipophilic local anesthetics from aqueous plasma or tissues or by counteracting local anesthetic inhibition of myocardial fatty acid oxygenation.[80,81]

The following is a summary of the cardiovascular complications of bupivacaine:

1. Bupivacaine is more cardiotoxic than is lidocaine.
2. Parturients may be more susceptible than nonpregnant patients to bupivacaine cardiotoxicity, but the mechanism is unknown.
3. *The resuscitation time following bupivacaine administration may be longer, and one must remember to relieve aortocaval compression by proper left uterine displacement.*
4. *Intravenous intralipid emulsions should be considered*
5. Epinephrine and atropine may be necessary in high doses.
6. Amiodarone should be the drug of choice for the treatment of ventricular tachyarrhythmias.
7. Amrinone may be the drug of choice to treat bupivacaine-induced myocardial depression.
8. If necessary, extracorporeal circulatory assistance is to be considered.

Differences Between Spinal and Epidural Anesthesia for Cesarean Delivery

Table 12-3 lists the differences between spinal and epidural anesthesia for cesarean delivery.

Table 12–3. Differences Between the Spinal and Epidural Anesthesia for Cesarean Delivery

Spinal Anesthesia	Epidural Anesthesia
Advantages	
Simple, rapid, reliable	Lesser incidence of hypotension
Minimal drug exposure	Avoidance of dural puncture
	Provide anesthesia for longer duration
	Use for postoperative analgesia
Disadvantages	
Hypotension	More complex procedure
Nausea and vomiting	Longer onset of time
Limited duration of action unless a continuous catheter technique is utilized	Large amount of local anesthetic required
Combined spinal and epidural anesthesia Advantages: Shortened recovery room stays if small amount of local anesthetic used for spinal block and less hypotension for the same reason	

Combined Spinal Epidural (CSE) Technique

The CSE technique has been popularized by a group from Sweden.[82] The authors suggested the following advantages of CSE technique: (1) speed of onset; (2) superior surgical analgesia and muscular relaxation; (3) lesser need for supplementary analgesics, sedatives, and antiemetics; (4) lower incidences of hypotension; (5) lower dose of local anesthetics in the mother and fetus; (6) blocking of sacral nerve roots due to use of

hyperbaric local anesthetic; (7) CSE block appears to combine the reliability of spinal block and the versatility of epidural block. If the CSE block is properly performed, this technique may be associated with all of the advantages mentioned by the author. Davies et al., conducted a randomized blind study comparing CSE technique with the epidural procedure. Their conclusions were both epidural anesthesia and CSE were associated with lower failure rates, with good operative conditions. However, CSE conferred high levels of maternal satisfaction. In addition, maternal advantages also included greater satisfaction after block placement before surgery, and reduced pain during delivery of the fetus in CSE group.[83] Some studies showed that spinal part of CSE technique was associated with a higher block compared to single-shot spinal technique for cesarean delivery. However, this was not proven in a more recent study where cerebrospinal fluid pressure was also monitored.[84] One of the distinct advantages of CSE technique is that it facilitates administering smaller amounts of local anesthetic agent (7–8 mg bupivacaine) and the epidural catheter can be used to augment the block further if indicated. This sequential combined spinal epidural anesthesia has been shown to decrease the degree of hypotension, and also associated with shorter recovery room stay.[85,86] This method has been used successfully for cesarean delivery in parturients with cardiac disease.[87,88]

General Anesthesia

The *advantages* of general anesthesia are as follows:

1. Speed of induction
2. Reliability
3. Reproducibility
4. Controllability
5. Avoidance of hypotension

The following are *disadvantages* of general anesthesia:

1. Possibility of maternal aspiration
2. Problems of airway management
3. Narcotization of the newborn
4. Maternal awareness during light general anesthesia

Complications of General Anesthesia

Maternal Aspiration

Since Mendelson recognized the importance of gastric pH in maternal aspiration, the necessity of neutralizing this acid has become apparent.[89] Roberts and Shirley reported the aspiration of gastric contents during anesthesia for cesarean delivery despite the previous administration of particulate antacids.[90] Another disturbing factor is the demonstration, in animals, that particulate antacids, if aspirated, may cause physiological and structural alterations in the lung. *Nonparticulate antacids* (0.3 M *sodium citrate or Bicitra*) *avoids this problem.*[91] Dewan and colleagues demonstrated the effectiveness of 30 mL of 0.3 M sodium citrate administered within an hour of induction of cesarean section. None of the parturients given sodium citrate had gastric aspirates at risk (pH < 2.5) of acid aspiration.[92]

Anticholinergics. Glycopyrrolate, an anticholinergic, has been advocated because of its ability to decrease gastric secretions. However, it can relax the gastroesophageal sphincter, and hypothetically increase the risk of regurgitation and aspiration.

Other Pharmacological Agents. The histamine (H_2) receptor antagonists cimetidine and ranitidine have been used to inhibit basal gastric acid secretion in order to increase the gastric pH and decrease gastric volume.[93] Metoclopramide, which increases gastric motility as well as esophageal sphincter tone, is a commonly used medication, especially for parturients undergoing cesarean section under general anesthesia[94] Metoclopramide also has a central antiemetic property related to its antidopaminergic action on the chemoreceptor trigger zone (CTZ).[95]

Airway Management

Parturients decrease arterial oxygen saturation faster than nonpregnant women (Table 12-4), and this is related to increased oxygen consumption and decreased functional residual capacity. Preoxygenation with 100% oxygen is absolutely essential before the induction of anesthesia. *Norris and Dewan compared two methods of preoxygenation: 100% oxygen for*

Table 12–4. Maternal Oxygen Tension in Pregnant and Nonpregnant Patients Following Apnea

	Parturient Women		Gynecological Patients	
Parameter	Before Apnea	After Apnea (1 min)	Before Apnea	After Apnea (1 min)
PaO_2 (mmHg)	473 ± 34*†	334 ± 43*†	507 ± 38	449 ± 40
$PaCO_2$ (mmHg)	31.4 ± 2.4	40.4 ± 2.7	35.6 ± 1.8	44.3 ± 1.1
pH	7.41 ± 0.02	7.33 ± 0.01	7.45 ± 0.02	7.35 ± 0.01

†$P < 0.05$.
From Archer et al.[151]

3 min vs. four maximal deep breaths in 30 s. The mean PaO_2 was not different between the groups.[96,97] Hence in a situation of acute fetal distress, four deep breaths of 100% oxygen may suffice. Pregnant women denitrogenate faster during preoxygenation; however, they also desaturate faster during apnea as compared to nonpregnant subjects.[97,98] Rapid sequence induction utilizing cricoid pressure (Sellick's maneuver) followed by endotracheal intubation is the routine induction procedure. American Society of Anesthesiologists monitoring standards should be followed in every case including capnography.

An additional hazard of general anesthesia could be a difficulty or impossibility of endotracheal intubation following the intravenous induction of anesthesia. This remains the major contributing factor to anesthesia-related maternal complications.[99,100] The incidence of failed tracheal intubation in the pregnant population is perhaps eight times higher than in the nonpregnant population.[101] The first national study of anesthesia-related maternal mortality in the United States revealed that 52% of the deaths resulted from complications of general anesthesia predominantly related to airway management problems.[102] Despite decreases in the number of obstetric general anesthetics and better awareness of obstetric airway difficulties, a recent survey study has shown that

the incidence of difficult intubation and subsequent complications have not diminished with time.[103] Furthermore, a critical evaluation of anesthesia-related maternal deaths in Michigan, 1985–2003, showed that airway obstruction or hypoventilation during emergence and extubation were the cause of five maternal deaths.[104] Obvious factors such as enlarged breasts have been implicated, but simple maneuvers for dealing with these problems did not seem to decrease the incidence of difficult intubation.[103,105,106]

Pilkington et al. demonstrated that the airway edema can increase during the course of pregnancy and result in increases in Mallampati score.[106] Furthermore, Kodali et al. have shown recently that the two components of upper airway (Samsoon's modification of Mallampati class, and pharyngeal volume) decrease during the course of labor.[107] Oral volume changes were observed by photographing the upper airway pre- and post-labor using a special camera (fig. 12-7a, b). The pharyngeal airway changes were demonstrated using acoustic reflectometry (Fig. 12-8). The relationship between increasing airway classification and relative ease or difficulty at intubation in term pregnant women undergoing cesarean delivery under general anesthesia were studied by Rocke et al.[108] The relative risk of encountering difficult intubation in pregnant women with a class 3 airway was 7.58 times more compared to parturients with class 1 airways during general anesthesia. This relative risk increased to 11.3 in pregnant women with a class 4 airway. This suggests that a change in airway class from 2 to 4 in parturients is associated with enhanced relative risk of encountering difficult intubation from 3.23 to 11.3. Therefore, women undergoing labor may be at increased risk of difficult intubation, particularly if labor is associated with airway changes. Hence, it is prudent to reevaluate the airway in women in labor presenting for cesarean delivery just prior to commencement of the anesthetic, rather than obtaining the information from the pre-labor evaluation data sheet. However, it must be remembered that the concealed portion of the upper airway, namely the pharyngeal volume, can also narrow during labor.[107]

If difficult intubation is encountered following induction of general anesthesia, it is essential that oxygenation should

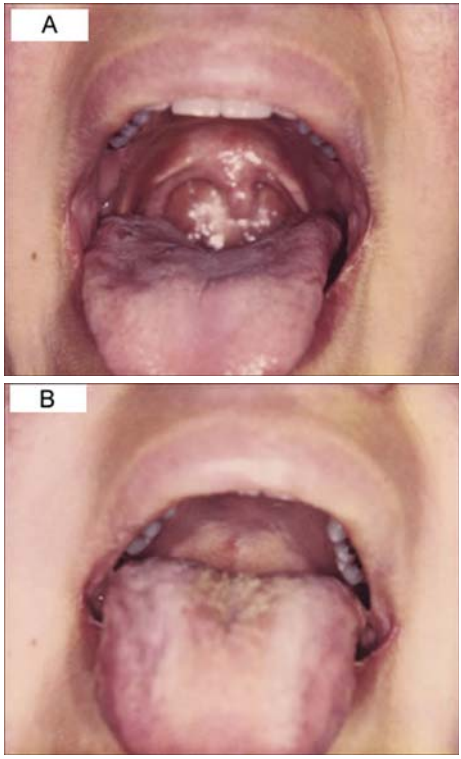

Figure 12–7. Airway pictures (**a**) pre-labor (Samsoon's modification of Mallampati class 1 airway), and (**b**) post-labor (Samsoon's modification of Mallampati class 3 airway). From Kodali [107] with permission.

be maintained by ventilating via mask. If there is no urgency such as continued fetal distress or antepartum hemorrhage, anesthesia may be discontinued and the woman may be allowed to wake up while the situation is assessed and an alternative anesthetic strategy is adopted. On the other hand, if it is deemed essential to continue anesthesia, laryngeal mask can be inserted to facilitate anesthesia.[109–111] Depending on

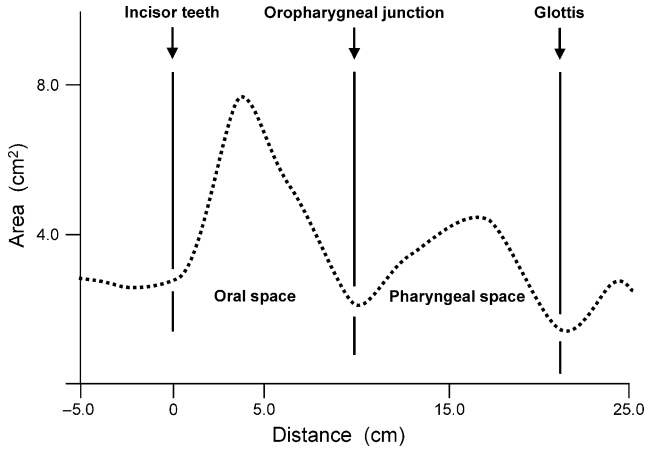

Figure 12–8. Acoustic reflectometry tracing showing various components of upper airway beginning from incisor teeth to glottis. (From Kodali et al.[107] Used with permission.)

the circumstances and available expertise/equipment, endotracheal tube can be inserted via fiber optic bronchoscope through the laryngeal mask airway under vision to minimize trauma to the airway. Laryngeal mask airway has also been successfully used in the instances of difficult intubation–difficult ventilation scenario. Laryngeal mask airway has also been placed under local anesthesia to act as a conduit for awake endotracheal intubation before induction of general anesthesia.[112] A means of instituting transtracheal ventilation should be immediately available in every obstetric suite if laryngeal mask airway does not restore access to airway. Patel described a system for delivering transtracheal ventilation. It consists of a 12- or 14-gauge intravenous catheter that will connect easily to the adapter of a 3-mm endotracheal tube. The end of this system can be attached easily to conventional anesthesia system.[113]

A difficult or failed intubation drill is extremely important, and every institution should have a plan before the situation

arises (Fig. 12-9). When a difficult intubation is suspected, close communication with the obstetrician and the woman is absolutely vital to make the final decision.

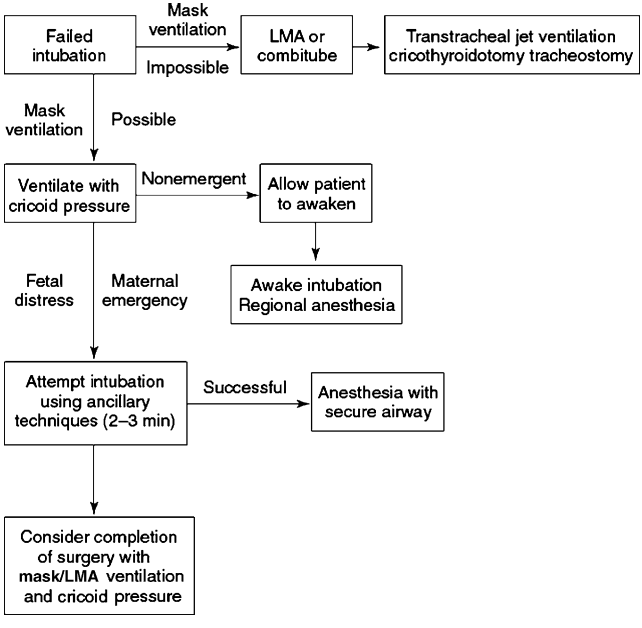

Figure 12–9. Steps in a drill when intubation is difficult during cesarean section. (Adapted from Malan and Johnson.[149])

Choice Between Regional and General Anesthesia when Difficult Airway Is Anticipated

Regional Anesthesia

Many anesthesiologists prefer either epidural or a continuous spinal technique when a difficult airway is anticipated. The technique should be instituted, if possible, before the onset of active labor.

The *advantages* of regional anesthesia include the following:

1. It can be used for an acute fetal distress situation without facing difficult intubation and thus promoting further fetal compromise.
2. The woman is awake, and thus there is less chance of gastric aspiration.
3. The continuous spinal technique can be induced in a very short time and can be used in situations where there is fetal distress.

Disadvantages of regional anesthesia include the following:

1. *Accidental intravascular injection with a possibility of convulsion, cardiovascular collapse, and aspiration.*
2. *Accidental subarachnoid injection causing total spinal anesthesia with the possibility of severe hypotension, unconsciousness, and aspiration. Obviously, in both these situations, ventilation with 100% oxygen will be absolutely essential and airway may have to be secured.*

General Anesthesia

The *advantages* of general anesthesia include the following:

1. *Airway is secured electively: Awake intubation by using either a laryngoscope or fiber-optic technique after anesthetizing the oral cavity with local anesthetic is the method of choice. Awake laryngeal mask insertion and endotracheal intubation is an alternative.*
2. *One can avoid the complications of regional anesthesia* (*accidental intravascular or subarachnoid injection*).

The following are *disadvantages* of general anesthesia:

1. It might take a longer time; hence, it may not be ideal in acute fetal distress situations.
2. Maternal discomfort while airway is being secured before general anesthesia.

Effect of General Anesthesia on the Baby

Causes of neonatal depression under general anesthesia can be classified as follows:

I. Physiological causes
   A. Maternal hypoventilation

B. Maternal hyperventilation
C. Reduced uteroplacental perfusion due to aortocaval compression

II. Pharmacological causes
A. Induction agents
B. Neuromuscular blockers
C. Low oxygen concentration
D. Nitrous oxide and other inhalational agents
E. Effect of prolonged induction-delivery and uterine incision-delivery intervals

Underlying Physiology

The physiological changes of pregnancy render the parturient more susceptible to rapid changes in blood gas tension. Hypoventilation will reduce the oxygen tension in the mother and in turn will cause neonatal acid–base alterations or biochemical depression. *Maternal hyperventilation may also impose potential harm to the fetus during general anesthesia by decreasing fetal oxygen tension. Mechanisms (Fig. 12-10)*

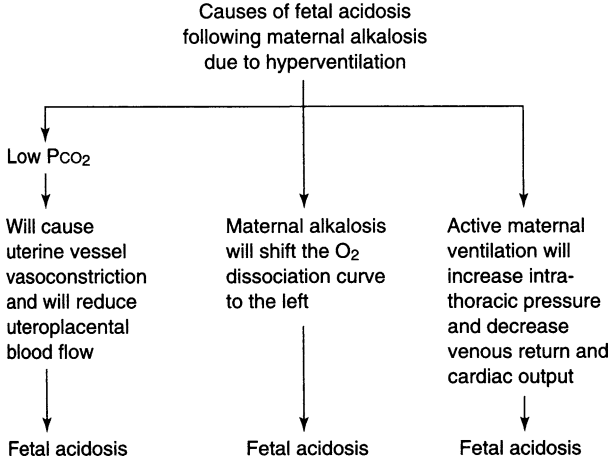

Figure 12–10. Causes of fetal acidosis following maternal alkalosis due to hyperventilation.

that have been invoked to explain this phenomenon[114] *include (1) vasoconstriction of umbilical vessels secondary to maternal hypocarbia, (2) altered maternal hemodynamics secondary to increased intrathoracic pressure during hyperventilation that causes a decrease in aortic and uterine blood flow, and (3) a shift of the maternal oxyhemoglobin dissociation curve to the left* (Fig. 12-11). Capnography is vital in preventing hypo- or hyperventilation. The arterial to end-tidal carbon dioxide gradient is decreased from the usual 4–5 mmHg in nonpregnant individuals to almost to zero in pregnancy, and hence

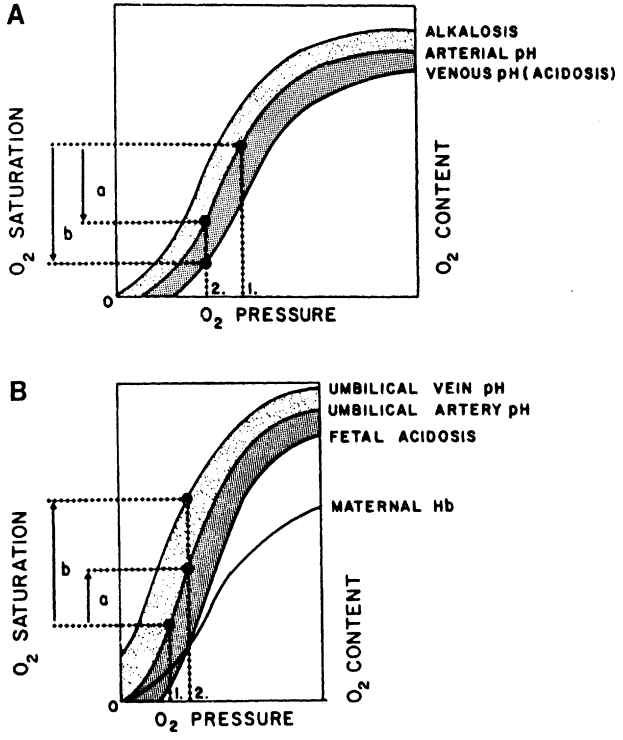

Figure 12–11. Hemoglobin dissociation curves of mother and fetus at the intervillous space and the importance of maternal PCO_2. A lower maternal PCO_2 will shift the curve to the *left*. (From Abouleish.[150] Used with permission.)

during cesarean section under general anesthesia end-tidal carbon dioxide reflects arterial carbon dioxide.[115] Maintaining end-tidal carbon dioxide around 32 mmHg is a reasonable approach in guiding ventilation during cesarean section under general anesthesia.

Aortocaval compression becomes more important when abdominal delivery is undertaken for suspected or documented fetal asphyxia. Increased asphyxia by permitting the patient to be supine will be highly detrimental to the fetus. Better fetal outcomes result from avoiding aortocaval compression. A left uterine tilt must be assured all the time.

Pharmacological Effects

Induction Agents. Standard practice is induction of anesthesia with an intravenous injection of thiobarbiturate, usually thiopental. The recommended dose is 4 mg/kg pregnant body weight. Thiobarbiturates cross the placenta rapidly and are detected in fetal blood within seconds of their administration to the mother (Fig. 12-12). *The concentration of umbilical vein blood remains lower than that of maternal vein blood;*

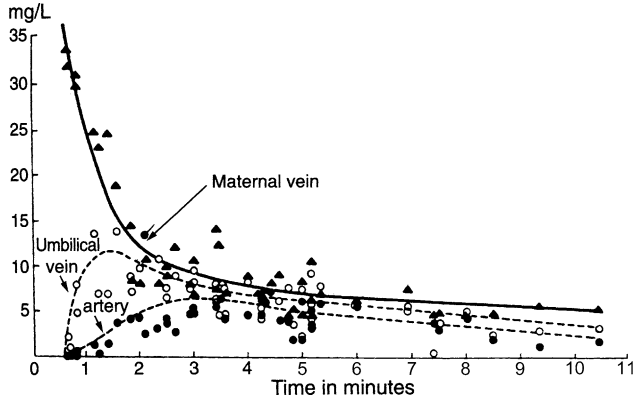

Figure 12–12. Thiamylal concentrations in the maternal vein, umbilical vein, and umbilical artery. (From Kosaka et al.[116] Used with permission.)

the concentration of umbilical artery blood is lower than that of umbilical vein blood.[116] *These gradients result from (1) a rapid decline in concentration of thiobarbiturate in maternal blood secondary to rapid redistribution, (2) nonhomogeneous distribution in the intervillous space, (3) extraction of thiobarbiturate from umbilical vein blood by the fetal liver, and (4) progressive dilution through shunting in the fetal circulation*. Ketamine (1–1.5 mg/kg) may be the induction agent of choice in the presence of hemorrhage. The nonbarbiturate induction agent propofol (2–2.5 mg/kg) did not show any significant advantage for cesarean section.[117–119] A combination of remifentanyl and propofol has also been used in selective cases such as Marfan's syndrome.[119] Etomidate (0.3 mg/kg) has been associated with less myocardial depression and greater hemodynamic stability and is the drug of choice in patients with cardiovascular compromise..[120,121]

Neuromuscular Blockers. Neuromuscular blockers are highly ionizable, and except in unusual circumstances, there is little observable effect on the newborn that can be attributed to muscle relaxants. Studies of *d*-tubocurarine, pancuronium, metocurine, and succinylcholine suggest that after a volume injection small quantities of these drugs may cross the placenta but maternal paralyzing doses do not affect the fetus. However, prolonged maternal and newborn neuromuscular blockade has been reported after the administration of succinylcholine to the mother.[122] This was due to the presence of atypical pseudocholinesterase in both the mother and newborn. Some authors recommend the administration of a small dosage of a nondepolarizing muscle relaxant *before the use of succinylcholine to prevent fasciculations and an associated increase in intragastric pressure*.[123] This concept is not agreed upon universally; opponents will not use any nondepolarizing muscle relaxants prior to the use of succinylcholine because (1) *parturients rarely exhibit fasciculations after succinylcholine;*[124] (2) *succinylcholine produces inconsistent and unpredictable elevations in intragastric pressure;*[125] (3) *succinylcholine tends to increase lower esophageal sphincter pressure in association with increased intragastric pressure, and thus the barrier pressure remains essentially unchanged;*[126]

(4) *intubation conditions may not be ideal if a nondepolarizing muscle relaxant is used prior to succinylcholine due to decreased efficacy of succinylcholine;* and (5) muscle pain after succinylcholine administration is far less following cesarean section than in nonpregnant subjects. Laudanosine, a metabolite of atracurium crosses the placenta and the mean placental transfer is 14% of maternal levels. Laudanosine levels are much lower with the cisatracurium and therefore should not affect the baby.[127]

Oxygenation. Fetal oxygenation is also affected by maternal inspired oxygen concentrations. A higher maternal inspired oxygen concentration will increase both maternal and fetal oxygen tensions and will improve the fetal condition at birth. For elective cesarean deliveries with no fetal distress, inspired oxygen concentration of 33–50% seems appropriate as there was no difference between the fetal oxygenations within this range of inspired oxygen concentrations.[128] Inspiratory oxygen concentration of 100% was associated with increased fetal oxygenation during elective cesarean delivery under general anesthesia. [129] Hence it may be prudent to use 100% inspiratory oxygen concentration for emergency cesarean delivery for fetal distress. Contrary to earlier reports, maternal hyperoxygenation does not result in fetal acidosis.

Nitrous Oxide. Nitrous oxide crosses the placenta rapidly and attains a fetal umbilical artery/umbilical vein concentration ratio of 0.8 after 15 min. The prolonged administration of nitrous oxide in high concentrations may result in low Apgar scores, possibly caused by direct CNS depression and diffusion hypoxia. Our current practice is not to exceed a nitrous oxide concentration of 50%. Mankowitz and his associates[130] have demonstrated that newborns whose mothers received nitrous oxide (50% oxygen and 50% N_2O with 0.6–1.0% enflurane) for cesarean delivery were largely unaffected at birth. However, they recommend (as do the authors) that all infants born to mothers who have received nitrous oxide before delivery receive oxygen or oxygen-enriched air, especially when the induction-to-delivery interval is prolonged, to further aid the infants in the adaptation from intrauterine to extrauterine life.

In the past, various inhalational agents have been used in combination with nitrous oxide, including halothane, methoxyflurane, trichloroethylene, enflurane (Ethrane), and isoflurane. All are reported to produce satisfactory anesthesia with few side effects. The current trend is to use isoflurane, and newer agents sevoflurane and desflurane with or without nitrous oxide (isoflurane 0.5% in 50% nitrous oxide, oxygen; sevoflurane 1% with 50% nitrous oxide, oxygen, or 1.5–2% in 100% oxygen: sevoflurane 1.5% keeps BIS score <60).[131–133] In one study, desflurane 2.5% in 50% nitrous oxide, oxygen had better neonatal condition than sevoflurane 1.5% in 50% nitrous oxide, oxygen.[134] However, in another study, general anesthesia for caesarean section with 4.5% desflurane in 50% nitrous oxide maintained BIS < 60 more often (statistically significant) than 3% of desflurane in 50% N_2O without maternal and neonatal adverse effects in healthy parturients.[135]

Effect of Induction-Delivery and Uterine Incision-Delivery Intervals. There is a difference of opinion about the optimal time for delivery of the infant when general anesthesia is used for cesarean delivery. Several authors found a better neonatal status when the induction-delivery interval was less than 10 min. Crawford et al. emphasized that if aortocaval compression is avoided, the inspired oxygen concentration is 65–70%, and there is no hypotension, then an induction-delivery interval as long as 30 min has no significant effect on the acid–base status of the newborn infants.[136] When Datta et al. used 50% nitrous oxide/50% oxygen and a small concentration of a volatile agent to produce amnesia, they found no significant effect on the acid–base values and Apgar scores when babies were delivered within 10 min.[137]

Another important factor related to the induction-delivery interval that may have considerable influence on the infant's condition is the duration of the uterine incision-delivery interval. In the absence of hypotension during spinal anesthesia, the length of the induction-delivery interval is not a factor in regard to neonatal outcome as measured by Apgar scores and neonatal acid–base values. However, uterine incision-delivery intervals longer than 180 s are associated with low Apgar scores as well as acidotic babies. During general anesthesia when

induction-delivery intervals were greater than 8 min or uterine incision-delivery intervals were greater than or equal to 180 s, lower 1-min Apgar scores (less than 7) and neonatal umbilical artery acidosis were present.[137] We also observed that prolonged uterine incision-delivery intervals during regional anesthesia resulted in elevated fetal umbilical artery norepinephrine concentrations and associated fetal acidosis.[138] An adverse outcome with prolonged uterine incision-delivery intervals may be the result of (1) the effects of uterine manipulations on uteroplacental and umbilical blood flows, (2) pressure of the uterus with accentuation of aortocaval compression, (3) compression of the fetal head during a difficult delivery, or (4) inhalation of amniotic fluid as a result of gasping respirations by the fetus in utero. The presence of increased norepinephrine concentrations in the fetus may be a sign of fetal hypoxia.

Maternal Awareness

A major problem with general anesthesia for cesarean delivery is the incidence of maternal awareness and unpleasant recall associated with the use of small doses and low concentrations of anesthetics to minimize neonatal effects. Incidences of recall have been reported to range from 17% to 36%. The use of low concentrations of potent volatile anesthetic agents will successfully prevent awareness and recall without adverse neonatal effect or excessive uterine bleeding.[139] As stated above, desflurane 4.5% or sevoflurane 1.5% in 50% nitrous oxide has been shown to assure BIS scores <60 during cesarean section general anesthesia. This can minimize the chances of awareness.

Summary of General Anesthesia for Cesarean Delivery

1. Premedication with metoclopramide, 10 mg intravenously, and nonparticulate antacid (30 mL of a 0.3 M sodium citrate solution)

2. Monitoring of blood pressure, pulse, ECG, O_2 saturation, capnography, temperature, nerve stimulator
3. Left uterine displacement
4. Preoxygenation with 100% oxygen
5. Induction with thiopental/ketamine/propofol and succinylcholine while maintaining cricoid pressure
6. Cuffed endotracheal tube
7. Fifty percent O_2, 50% N_2O with a small amount of isoflurane (0.75%), enflurane (1%), desflurane (4%), or sevoflurane (1.5%) unless contraindicated
8. Avoidance of hypoventilation or hyperventilation, maintain end-tidal carbon dioxide around 32 mmHg.
9. Muscle relaxants: either a 0.1% succinylcholine infusion or nondepolarizing muscle relaxants (vecuronium 4 mg) with the use of a neuromuscular blockade monitor.
10. Desufflation of the stomach by a gastric tube after induction and intubation
11. Minimization of the induction-delivery interval
12. Minimization of the uterine incision-delivery interval
13. Use of narcotics in the mother after delivery of the baby
14. Extubation performed when the mother is wide awake

Air Embolism During Cesarean Delivery

A mention of air embolism during cesarean delivery needs emphasis in this chapter because of its high incidence during cesarean delivery. The incidence of venous air embolism during cesarean delivery has been reported to be between 9.5% and 65%,[140,141] and this can happen during epidural, spinal, and general anesthesia. Air emboli in the pulmonary circulation may cause a ventilation/perfusion mismatch and can lower oxygen saturation.[142] Chest pain and dyspnea may be associated with venous air embolism, and ECC changes have also been observed. The majority of changes have been noted with uterine incision and delivery[140] as well as at the time of uterine exteriorization.[143] Hence, oxygen saturation, blood pressure, and pulse should be closely monitored during delivery and immediately postpartum.

Postoperative Pain Relief

Intravenous Method

Patient-controlled analgesia (PCA) has become a popular method for postoperative pain relief following general anesthesia for cesarean section. Morphine remains the drug of choice for this purpose.[144] Sinatra and colleagues compared morphine, meperidine, and oxymorphone for PCA and observed a rapid onset and less sedation, nausea, vomiting, and pruritus with meperidine.[145] However, the same group reported neonates whose mothers received meperidine for PCA scored lower in the neurobehavioral scoring system than did the morphine-treated group.[146] A significant amount of normeperidine was found in the breast milk of the mothers who received meperidine. The authors concluded that PCA with morphine for pain relief following cesarean section provided equivalent maternal analgesia and overall satisfaction to that provided by PCA with meperidine, but with significantly less neurobehavioral depression among breast-fed neonates on the third day of life. One should not expect such problems if meperidine PCA is not used for more than 24 h.

Neuraxial Narcotics

As already stated, preservative free morphine (0.2 mg spinal or 3 mg epidural) provides satisfactory pain relief for 18–24 h. Palmer et al. described the dose–response relationship of epidural morphine for postcesarean analgesia for quality of analgesia and relation to the side effects of pruritus, nausea, and vomiting in 60 term parturients undergoing nonurgent cesarean delivery. The patients received a single dose of epidural morphine after delivery (0 mg, 1.25 mg, 2.5 mg, 3.75 mg, or 5 mg). The quality of analgesia increased as the dose of epidural morphine increased to at least 3.75 mg; increasing the dose further to 5 mg did not improve analgesia. Side effects were not dose related.[54] Based on this study and others, the general practice is to use 3 mg morphine epidurally.[71] However, it is prudent to monitor respiratory rate following their use

in the postoperative period to detect a rare event of delayed respiratory depression. Kato et al. retrospectively evaluated parturients receiving 0.15 mg intrathecal morphine for cesarean delivery for bradypnea (respiratory rate $\leq$ 10 breaths/min) within 24 h after the intrathecal injection. Of 1915 patients, 5 women (0.26%) developed bradypnea (respiratory rate $\leq$ 10 breaths/min) during the 24 h period. The incidence of severe bradypnea (oxygen desaturation below 90% and 30-s apneas requiring naloxone) was 1/1915 (0.052%).[147] Therefore, our practice is to monitor hourly respiratory rate in the postoperative period for 18–24 h. We also use neuraxial narcotics in morbidly obese parturients to avoid intravenous narcotics. The patients are, however, kept under close surveillance at least for a day.

Summary

Our understanding of the physiology, pharmacology, and clinical management of anesthesia for cesarean delivery has greatly advanced in recent years. If the basic principles about various techniques described in this chapter are adhered to, one should expect an excellent maternal and fetal outcome with either general or regional anesthesia in the normal parturient.

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13
Neonatal Resuscitation

Most neonates require only basic supportive care at the time of delivery. Approximately 10% will need brief respiratory support, and 1% will require extensive resuscitative efforts.[1] The vast majority will adapt to extrauterine life with only minimal assistance from delivery personnel.

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Physiologic Adaptation to Extrauterine Life

A discussion of physiological adaptations of neonates at the time of delivery is important to understand the goals and techniques of neonatal resuscitation.

Cardiovascular System

Gas exchange occurs in fetus from the mother via the placenta. Ten percent of maternal cardiac output reaches the placenta. Oxygenated blood returns to the fetus via the umbilical vein; 50% of the umbilical vein flow enters the inferior vena cava via the ductus venosus, and the other half enters the hepatoportal system (Fig. 13-1). A streaming phenomenon tends to separate blood with higher oxygen saturation such that it flows preferentially to the left atrium via the foramen ovale, whereas relatively deoxygenated blood enters the right atrium. Blood ejected from the left heart is responsible for supplying oxygenated blood (saturation approximately 65–70%) to the brain and upper extremities. Less oxygenated blood from the right atrium (saturation approximately 55%) flows to the right ventricle and most returns via the ductus arteriosus to the systemic circulation; it perfuses the lower half of the body and approximately 40% returns to the placenta via the umbilical artery where it is reoxygenated. Oxygen saturation, oxygen and carbon dioxide tension, and pH of umbilical venous and arterial blood are shown in Table 13-1. Several factors contribute to ensure adequate oxygenation at the low PO_2 of the fetal blood. First, the relatively fast fetal heart rate and the decreased systemic vascular resistance of the placenta maintain the high fetal cardiac output relative to total body surface area. Second, the fetal hemoglobin concentration is higher than the adult, approximately 16 g/dL. Third, fetal blood will show a higher oxygen saturation as compared with adult blood at the same oxygen tension. This is due to differences in the affinity of fetal hemoglobin for oxygen, in turn due to lower binding of 2,3-diphosphoglycerate (2,3-DPG) to fetal hemoglobin. This shifts the hemoglobin–oxygen dissociation curve to the left (Fig. 13-2). The P_{50} (the PO_2 corresponding to 50% saturation)

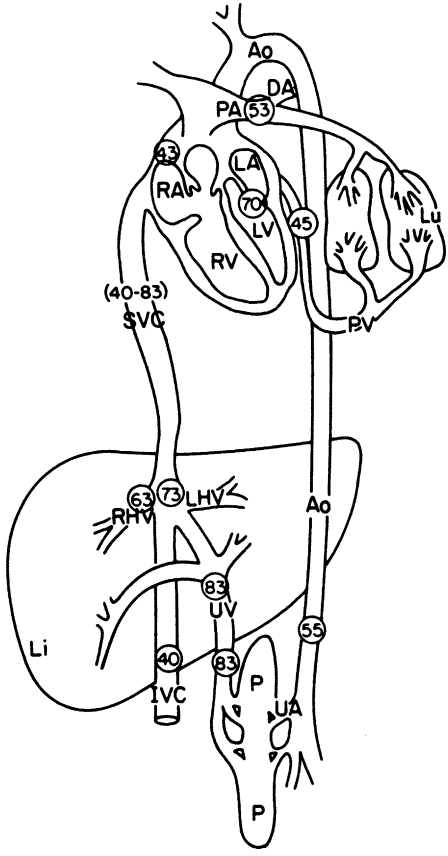

Figure 13–1. Fetal circulation with oxygen saturation in different parts of the fetus (*circled numbers* indicate percent saturation). *P* = placenta; *IVC* = inferior vena cava; *UV* = umbilical vein; *RHV* = right hepatic vein; *LHV* = left hepatic vein; *SVC* = superior vena cava; *RV* = right ventricle; *RA* = right atrium; *LV* = left ventricle; *LA* = left atrium; *PA* = pulmonary artery; *DA* = ductus arteriosus; *AO* = aorta; *PV* = pulmonary vein; *AO* = aorta; *UA* = umbilical artery. (From Martin.[11])

of fetal hemoglobin at term is approximately 19–21 mmHg compared to 26–27 mmHg in the adult.

Table 13–1. Fetal Blood Gas and Acid–Base Values

	pH	PCO_2	PO_2	HCO_3^-
Umbilical artery	7.28 ± 0.05	49.2 ± 8.4 (50)	18.0 ± 6.2 (20)	22.3 ± 2.5
Umbilical vein	7.35 ± 0.05	38.2 ± 5.6 (40)	29.2 ± 5.9 (30)	20.4 ± 2.1

Data from Yeomans et al.[12] from 146 uncomplicated vaginal deliveries. Values are shown as mean ± SD. In parentheses are approximations of the mean values which form a convenient mnemonic: 20-30-40-50.

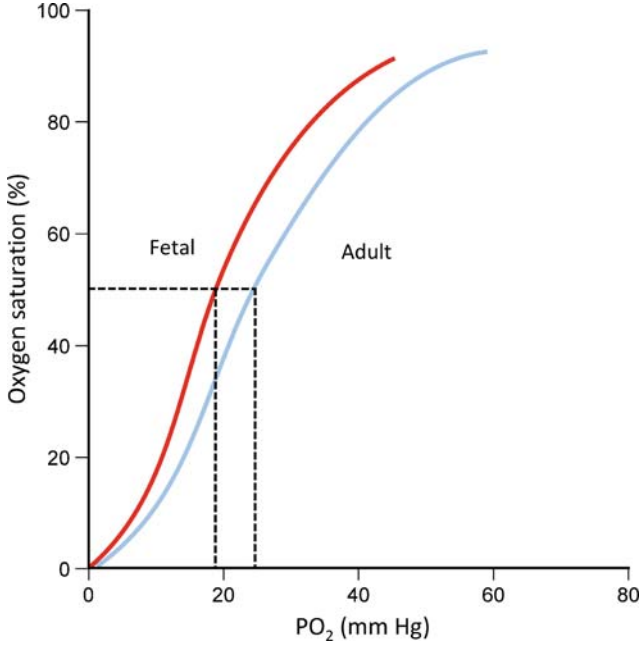

Figure 13–2. Adult and fetal oxyhemoglobin dissociation curves. The dotted line shows the P_{50}, the PO_2 associated with 50% saturation of hemoglobin. Fetal hemoglobin is more avid for oxygen and thus has a lower P_{50}.

At the time of delivery several changes take place: the onset of respiration increases fetal PO_2 and consequently decreases pulmonary vascular resistance; simultaneously, exclusion of the placental circulation by clamping the umbilical cord increases systemic vascular resistance. Increased systemic vascular resistance causes the closure of the foramen ovale, and the ductus arteriosus closes as a result of the increased fetal arterial PO_2.[2]

Respiratory System

In intrauterine life the fetal tracheobronchial tree is filled with approximately 30 mL/kg of fluid, which is an ultrafiltrate of plasma. At the time of birth the fetal lung fluid is cleared by several factors: (1) during vaginal delivery the fluid is squeezed out by compression of the thoracic cage, (so babies delivered by cesarean section will have more lung fluid because of the absence of this mechanism), (2) one-third of the lung fluid will be absorbed by lymphatics, (3) some of the fluid will be expelled by the newborns themselves, and (4) some of the fluid is deliberately suctioned out at the time of delivery.

Initiation of respiration is essential for the transition away from the fetal circulation and usually occurs within a few seconds to 1 min after delivery. Regular rhythmic respiration is established within 2–10 min. The exact stimulus responsible for the establishment of neonatal respiration is unknown; however, several factors may be involved: (1) squeezing of the thoracic cage by the vaginal canal and elastic recoil of the chest wall, (2) hypoxia and hypercarbia, (3) tactile stimulation, (4) umbilical cord clamping, and (5) possibly the lower temperature outside the uterus.

The first breath requires an extremely high negative intrathoracic pressure that can vary from 40 cm to 100 cm H_2O. The lungs are expanded with 40–70 mL of air, but expiration is incomplete, and the lungs become completely inflated after the first few breaths. Normal term neonates breathe 30–60 times per minute with a 10–30-mL tidal volume, and the lungs maintain a minute volume of about 500 mL.

During development the fetal lung produces two types of epithelial cells. Type II cells are responsible for the production of surfactant (surface-acting material), which is important for counteracting the surface tension and keeping the alveoli open. Surfactant production by type II cells begins by 22–24 weeks but is not complete until 34–38 weeks, putting preterm infants at risk of respiratory distress syndrome.

Thermoregulation

The neonate is unable to maintain body temperature by shivering, and hence nonshivering thermogenesis becomes an important factor.[3] Breakdown of brown fat is the main source of maintenance of fetal body temperature. The term fetus stores abundant brown fat in the neck, interscapular area, back, and axillary area as well as around different abdominal viscera, especially the kidney and adrenals. Brown fat is extremely vascular and receives as much as 25% of the cardiac output in hypothermic conditions. Cold stress will liberate norepinephrine, which is important for the metabolism of brown fat; this complex process involves an exothermic reaction that liberates heat with the utilization of a significant amount of oxygen.[4] Maintenance of body temperature is extremely important for the neonate because cold temperature will cause pulmonary vasoconstriction, increased right-to-left shunt, hypoxemia, and metabolic acidosis, which will further increase the right-to-left shunt.

General Principles of Neonatal Resuscitation

Several general principles should guide anesthesiologists' participation in newborn resuscitation. First, both ASA and ACOG agree that anesthesiologists should be primarily responsible for maternal well-being; hence, when active neonatal resuscitation becomes necessary, a person other than the anesthesiologist should be responsible for this task.[5] However, practices in this

regard will necessarily vary among institutions due to availability of staff trained in newborn resuscitation. Second, although most infants require little resuscitation, prior knowledge of a difficult delivery or delivery of a high-risk fetus will help predict the large majority of babies who will. Factors that may predict need for more aggressive resuscitation are listed in Table 13-2. Third, proper preparation includes ready availability of equipments, fluids, and medications (Table 13-3).

Table 13–2. Factors Associated with Need for Neonatal Resuscitation

Maternal factors
- Uteroplacental insufficiency
  - Diabetes mellitus
  - Preeclampsia
  - Postmaturity
  - Intrauterine growth retardation
  - Cocaine addiction
  - Autoimmune disease
- Fever and infection
- Hemorrhage
  - Placenta previa
  - Abruptio placentae
  - Ruptured uterus
  - Vasa previa
- Endocrine problems
  - Hypothyroidism or hyperthyroidism
  - Hypoadrenalism or hyperadrenalism
  - Pheochromocytoma
- Maternally administered drugs (high dose or overdose)
  - Opioids (particularly within 4 h of delivery)
  - Sedatives and tranquilizers
  - Magnesium sulfate
  - Local anesthetics
  - Calcium channel blockers
  - β-Blockers

Difficult deliveries
- Traumatic
  - Intrauterine manipulation
  - Breech extraction
  - Forceps delivery
  - Uterine hyperstimulation
  - Precipitous labor or delivery
  - Prolonged labor
  - Prolonged second stage
  - Prolonged rupture of membranes
  - Nonreassuring fetal heart rate tracing
  - Shoulder dystocia

Fetal factors
- Prematurity
- Small for dates
- Macrosomia
- Polyhydramnios or oligohydramnios
- Abnormal presentation, e.g., breech
- Multiple gestation
- Congenital anomalies
- Intrapartum fetal distress
- Presence of meconium
- Prolapsed umbilical cord

Table 13–3. Equipment and Medications Necessary for Neonatal Resuscitation

I. Radiant warmer
II. Equipment for suction
  A. Bulb syringe
  B. De Lee mucus trap with a 10-F catheter or mechanical suction
  C. Suction catheters, 5 F, 6 F, 8 F, and 10 F
  D. An 8-F feeding tube and a 20-mL syringe
  E. Adaptor for suctioning via endotracheal tube
III. Bag and mask
  A. Resuscitation bag with a pressure-release valve
  B. Face masks of different sizes
  C. Laryngeal mask airway
  D. Oral airways of different sizes
  E. Oxygen with a flow meter and tubing
IV. Equipment for intubation
  A. Laryngoscope with straight blades (#0 and 1)
  B. Endotracheal tubes (2.5 mm, 3.0 mm, 3.5 mm, and 4.0 mm)
  C. Stylet
  D. LMA (#1)
  E. Scissors
  F. Gloves
  G. Capnometer or chemical CO_2 detector
V. Medication and intravenous fluid
  A. Epinephrine, 1:10,000
  B. Naloxone hydrochloride (0.4 or 1 mg/mL)
  C. Albumin, 5% solution
  D. Normal saline
  E. Ringer's lactate
  F. Sodium bicarbonate (4.2% in 10-mL)
  G. Dextrose, 10%
  H. Sterile water
  I. Normal saline
  J. 5-F feeding tube or specialized umbilical vein catheterization tray

Evaluation of the Neonate: The Apgar Score

In 1953 Dr. Virginia Apgar devised a scoring system for quick evaluation of the neonate immediately after delivery[6] (Table 13-4). Scores are evaluated by observing five criteria and are recorded at 1 min and 5 min routinely. In severely

Table 13–4. Apgar Scoring System

Mnemonic (APGAR)	Sign	Score 0	Score 1	Score 2
Appearance	Color	Blue, pale	Pink body, blue extremity	Pink all over
Pulse	Heart rate	Absent	< 100 BPM	> 100 BPM
Grimace	Reflex irritability	No response	Some response, grimace	Cry, cough
Activity	Muscle tone	Flaccid	Some flexion	Active motion
Respiration	Respiratory effort	Absent	Slow, irregular	Strong cry

depressed infants, scores are recorded every 5 min for 20 min or until two successive scores are ≥ 7. If the 10-min score is 0, survival is rare (less than 2%).[7] However, higher scores have relatively weak long-term prognostic significance. Importantly, the Apgar score *should not be a guide to neonatal resuscitative efforts, which often begin well before 1 min of life, but should be viewed instead as a gauge of resuscitation efficacy.*[1]

Steps in Neonatal Resuscitation

Neonatal resuscitation proceeds according to a basic algorithm based on ongoing assessment of the newborn's respiration and circulation (Fig. 13-3). Vigorous term infants require little more than drying and warming, clearing of the airway by gentle bulb suctioning, and ongoing assessment. All newborns should be placed under a radiant warmer with a slight head-down tilt and the head slightly extended, and then gently dried. Infants that are not vigorous require progressively aggressive maneuvers to establish and maintain the airway, support respiration, and maintain adequate circulation. The mnemonic "A-B-C-D" (Airway, Breathing, Circulation, Drugs) helps remind the resuscitator of the preferred sequence of steps.

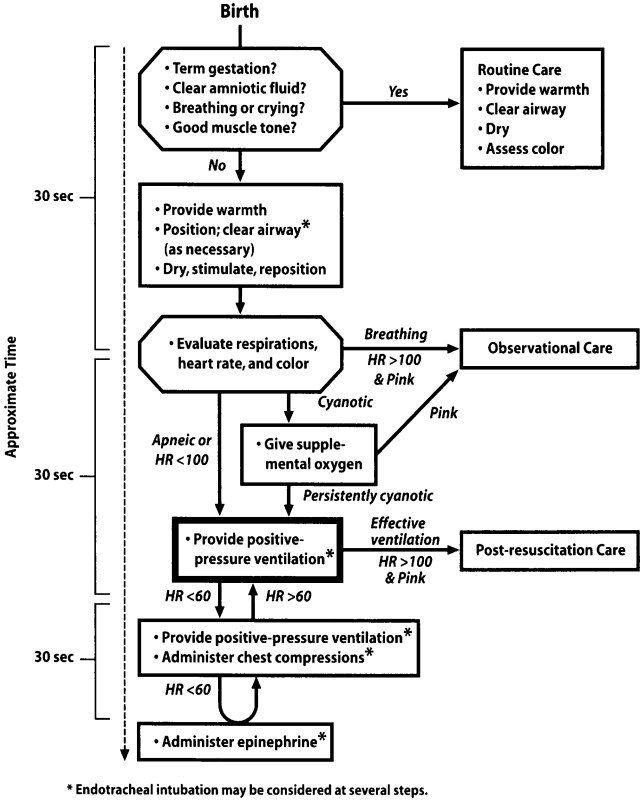

Figure 13–3. Basic algorithm for neonatal resuscitation. (From Tegtmeyer.[1] Used with permission.)

Airway

The first important step is clearing and establishing an open airway. Suction should begin shortly after the delivery by the obstetric team. Turning the head to the side will allow better drainage and removal of the secretion. Suction with a bulb syringe will be satisfactory in most cases, but *caution should be*

used to prevent stimulation of the posterior portion of the pharynx during the first few minutes after delivery to prevent vagally mediated bradycardia. The mouth is suctioned before the nose ("M before N"). In the presence of meconium-stained fluid, thin or thick, modern resuscitation algorithms are much more conservative than in the past, and depend on the overall condition of the neonate (Fig. 13-4). If the infant has absent or depressed respiration, decreased muscle tone and heart rate below 100, direct laryngoscopy should be done for suction of meconium from hypopharynx as well as from trachea. A special adaptor allows suction to be applied directly to the endotracheal tube after intubation of the trachea. Care should be taken to use moderate negative pressure, less than –100 mmHg. Suctioning can be repeated if meconium is aspirated but positive-pressure ventilation should be considered if the heart rate remains below 100. Gastric suction is also recommended after other initial resuscitation efforts are complete. If the infant is vigorous,

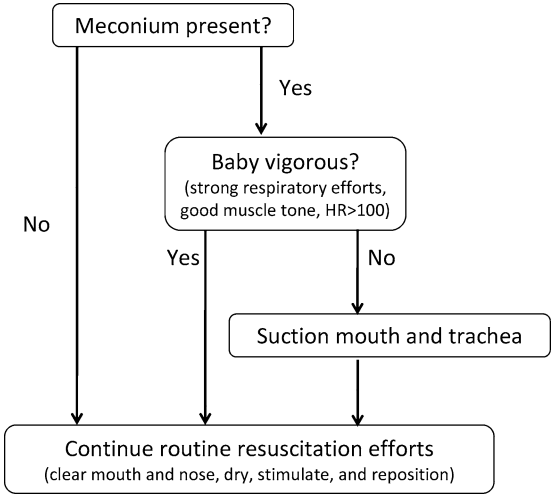

Figure 13–4. Treatment for meconium-stained amniotic fluid. (Redrawn and adapted from Tegtmeyer.[1])

regardless of the consistency of meconium, laryngoscopy and tracheal suction should not be performed.[1,8]

Breathing

Once the oral cavity is cleared, the majority of neonates will start breathing spontaneously, but in a few cases tactile stimulation may be necessary to initiate respiration. In the absence of respiratory effort and movement, positive-pressure ventilation using a bag and mask should be initiated. The heart rate should also be checked at the same time; adequate oxygenation with proper ventilation will improve the heart rate as well as the color. Most neonatal resuscitation bags have a built-in pressure-release valve that is set to release at 30–35 cm H_2O. Neonates should be ventilated at a rate of 40–60 per minute. The adequacy of chest movement should be observed and also be confirmed by listening for bilateral breath sounds. If the heart rate and color do not improve after adequate ventilation or if there is any difficulty in ventilation, endotracheal intubation may be necessary. The laryngeal mask airway can be used for ventilation if bag and mask ventilation is inadequate or endotracheal intubation is not successful or available.

Recent data suggest that the traditional practice of ventilating with 100% oxygen may not be optimal during neonatal respiration. Two recent meta-analyses of randomized trials involving over 3,000 infants receiving room air or oxygen during newborn resuscitation concluded that room air was superior with respect to mortality and trended towards a reduction in ischemic encephalopathy.[9,10] However, the American Heart Association guidelines do not yet call for substitution of room air for oxygen, but suggest both are acceptable. If room air is used first, and the heart rate does not improve, oxygen is recommended.[1]

Circulation

If the heart rate is below 60 beats per minute despite stimulation (rubbing and drying) and 30 s of positive-pressure ventilation, external cardiac compression should be started. Chest compression will compress the heart against the spinal

column, and this will help to maintain circulation in the vital organs. There are two techniques for external cardiac massage. In the thumb technique the fingers encircle the chest, with the thumbs lying over the midsternum and the fingertips lying over the spine. The sternum is compressed one-third of the anterior-posterior diameter of the chest, 90 times per minute. In the two-finger technique the tips of the middle finger and either the index finger or ring finger of the same hand are used to compress the sternum; the other hand can support the back of the neonate in the absence of a rigid surface. The sternum is again compressed one-third of the anterior-posterior diameter of the chest, 90 times per minute. Ventilation should be continued at 30 breaths per minute. Endotracheal intubation should be considered in order to facilitate ventilation during chest compressions. If the heart rate increases to >60 BPM, chest compressions can be stopped and ventilation increased to 40–60 breaths per minute. Ventilation can be gradually withdrawn when the heart rate increases to >100 BPM.

Drug Therapy

In the absence of improvement in the heart rate despite effective ventilation and 30 s of chest compressions, drug therapy is indicated.[1] Epinephrine is the preferred first-line drug, and is given intravenously by umbilical catheter at a dose of 0.1–0.3 mL/kg of a 1:10,000 solution. The umbilical vein should be the preferred route: a catheter is introduced through the umbilical stump until the tip of the catheter is just deep enough to allow free aspiration of blood. Threading the catheter too far will entail the risk of infusion of the solutions into the liver and risk liver damage. If the intravenous route is not available, epinephrine can be given via the endotracheal tube at a higher dose (up to 1 mL/kg). However, lower blood levels are obtained and effectiveness is uncertain.

Indications for Volume Expanders

Volume expanders are rarely indicated but may be considered in the following situations:

1. Persistence of pallor after adequate oxygenation
2. Presence of weak pulses or delayed capillary refill
3. Inadequate response to resuscitative measures
4. History consistent with blood loss (placental abruption or previa, vasa previa, bleeding from umbilical cord)

Normal saline or Ringer's lactate, 10 mL/kg over 5–10 min, is the preferred initial choice.

If there is acute bleeding or suspected anemia, whole blood (O-negative blood, which can be cross-matched with the mother's blood, where any reactive antibodies would originate, if time allows) is given at a similar dose.

Other Drugs

Other drugs are very rarely indicated in neonatal resuscitation. Recommended doses are shown in Table 13-5. Use of bicarbonate is discouraged. If it is used following prolonged arrests unresponsive to other medications, it should be used only after establishment of adequate ventilation and circulation. Continued use of bicarbonate should be associated only with documented fetal metabolic acidosis or hyperkalemia. A 4.2% solution at a dose of 2 mEq/kg is used, and it is given slowly at a rate of 1 mEq/kg/min. The risk of intraventricular hemorrhage following bicarbonate infusion can be minimized by using dilute solution (4.2%) and injecting slowly. Naloxone can be used in the presence of neonatal respiratory depression following maternal opioid administration within 4 h of delivery. It is given in a dose of 0.1 mg/kg intravenously, or intramuscularly; the intratracheal route is no longer recommended. *Naloxone should not be administered to a newborn infant whose mother is a chronic opioid user because of the possibility of precipitating acute withdrawal.*

Unusual Specific Causes of Neonatal Respiratory Problems

These rare conditions are classified by parts of the respiratory system.

Table 13–5. Medications for Neonatal Resuscitation

Medication	Concentration	Dosage route	Rate/ Precautions
Epinephrine	1:10,000	0.1–0.3 mL/kg IV or ET	Give rapidly May dilute with normal saline to 1–2 mL (ET)
Volume expanders	Whole blood 5% Albumin-saline Normal saline Ringer's lactate	10 mL/kg IV	Give over 5–10 min
Sodium bicarbonate	0.5 mEq/mL (4.2% solution)	2 mEq/kg IV	Give slowly, over at least 2 min Give only if infant is being effectively ventilated
Naloxone hydrochloride	0.4 mg or 1 mg/mL	0.1 mg/kg IV, ET, IM, SQ	Give rapidly IV (preferred), IM, ET not recommended
Dopamine	Varies by institution	5 mcg/kg/min may increase to 20 mcg/kg/min if necessary	Give as a continuous infusion using an infusion pump, monitor heart rate and blood pressure closely, seek consultation

I = intravenous, ET = endotracheal,IM = intramuscular, SQ = subcutaneous.

Choanal Atresia

This condition is associated with anatomic obstruction of the nasal passage. Attempted breathing via the nose will demonstrate an absence of breath sounds, and the newborn will be cyanotic. Breathing via the mouth or crying will make the baby pink, and breath sounds will be present.

There is an inability to pass a soft rubber or plastic catheter through the nose. Imaging after injection of a small amount of contrast media through the nares will confirm the anatomic obstruction. Choanal atresia is treated by insertion of a rubber or plastic oral airway and, if necessary, an endotracheal tube.

Upper Airway Obstruction

The Pierre Robin syndrome can cause neonatal respiratory problems and is a congenital malformation associated with

glossoptosis, micrognathia, and possibly a cleft palate. Clinical findings include sternal retraction, cyanosis, and specific congenital anomalies. Initial treatment may include pulling the tongue anteriorly, insertion of an oral airway or endotracheal tube (which may be very difficult), placement of a small endotracheal tube via the nose into the pharynx, and use of the prone position.

Anomalies of the Larynx

This can include webs, fusions, atresia, and vocal cord paralysis. Clinical findings include stridor, cyanosis, and prolonged inspiration and expiration. Placement of an endotracheal tube distal to the obstruction will alleviate the clinical problems. Expertise in the neonatal airway and facility with fiberoptic techniques may be required.

Anomalies of the Trachea

These include subglottic stenosis, tracheal rings, hemangiomas and webs, vascular rings, and tumors. Clinically, these anomalies may be characterized by inspiratory stridor, retraction, decreased breath sounds, collapse of the trachea during inspiration in the presence of incomplete tracheal rings, or tracheal bleeding in the presence of hemangiomas. An endotracheal tube should be inserted beyond the site of obstruction if possible. If there is pulmonary hemorrhage because of trauma to the hemangioma, the situation can be life-threatening. A neonatal airway expert and thoracic or ENT surgeon should be consulted.

Diaphragmatic Hernia

Diaphragmatic hernia is a congenital defect in the diaphragm with entrance of the gut into the thoracic cavity. It is usually diagnosed antepartum by ultrasound but may be discovered in the immediate neonatal period. Clinical findings include scaphoid abdomen, cyanosis, intercostal retractions, and grunting. Intubation of the trachea and the use of positive-pressure ventilation is usually started immediately after delivery. Careful ventilation is necessary because excessive pressure

may cause pneumothorax. Surgical intervention will be needed in these cases.

Pneumothorax

A collection of air in the pleural cavity (pneumothorax) can occur spontaneously or during ventilation with high pressure in situations like respiratory distress syndrome or meconium aspiration syndrome. Clinical findings include tachypnea, cyanosis, reduced breath sounds on the affected side, displacement of the trachea, and hypotension. An endotracheal tube in the right mainstem bronchus can also cause absent breath sounds on the left side and must be distinguished from pneumothorax in intubated infants. The diagnosis is confirmed by a chest X-ray, transillumination of the chest, or insertion of a needle or chest tube. Removal of air by a chest tube or intravenous catheter will be necessary in symptomatic cases.

Summary

Most deliveries remain uncomplicated and do not require extensive resuscitation of the infant. However, knowledge of neonatal resuscitation may become important, particularly in high-risk situations. Basic techniques centered on maintenance of the airway and ventilation are effective in almost all cases, with cardiovascular support and drug therapy only rarely required.

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14
High-Risk Pregnancy: Maternal Comorbidity

S. Datta et al., *Obstetric Anesthesia Handbook*,
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Modern medicine has increased the longevity as well as the functional status of women who have systemic diseases. This has resulted in many women reaching childbearing age with successful pregnancies. In vitro fertilization has its own impact in this phenomenon. The end result is a steady increase in the number of women requiring high-risk obstetric and anesthetic care to successfully maneuver these individuals through pregnancy, labor, and delivery. This chapter will focus on pathophysiology of various comorbid conditions one might encounter during obstetric anesthetic practice, and how it influences the anesthetic management.

Endocrine Disorders

Diabetes Mellitus

The major problems encountered in diabetic pregnancy are as follows:

1. Placental insufficiency
2. Superimposed preeclampsia
3. Diabetic nephropathy
4. Diabetic ketoacidosis is the main factor in the increased incidence of perinatal morbidity and mortality. Evidence exists that ketones can readily cross the placenta, and this can significantly decrease fetal oxygenation. Biochemical findings include a plasma glucose level greater than 300 mg/dL, plasma HCO_3 less than 15 mEq/L, arterial pH less than 7.30, and serum acetone positive at 1:2. The treatment of diabetic ketoacidosis should include enough insulin to correct the acidosis and to carefully balance the fluid, glucose, and electrolyte levels. Continuous fetal heart rate monitoring should be instituted for fetal surveillance.

Pathophysiological Changes

The anesthetic management of diabetic parturients should be based on the understanding of pathophysiological changes associated with diabetic pregnancy.

Deranged Uteroplacental Blood Flow. Maternal diabetes is associated with placental abnormalities even in the case of mild, well-controlled gestational diabetes. The uteroplacental blood flow index is reduced 35–45% in diabetic parturients. The blood flow index tends to be further impaired in those diabetic women who have higher blood glucose values.[1]

Impairment of Oxygen Transport in Diabetes. HbA_{1c} (a minor variant of hemoglobin A) levels are two to three times higher in insulin-treated diabetics than in control subjects. In contrast to hemoglobin A, the oxygen affinity of HbA_{1c} is little affected by the in vitro addition of 2,3–diphosphoglycerate (2,3–DPG). It has been observed that red blood cell oxygen transport, saturation, and tension are impaired in insulin-dependent diabetic subjects. *In poorly regulated women, in whom the concentrations of HbA_{1c} are higher and the concentrations of 2,3–DPG tend to be lower, the blood oxygen release at the tissue level may be more impaired*[2] (Figs. 14-1 and 14-2).

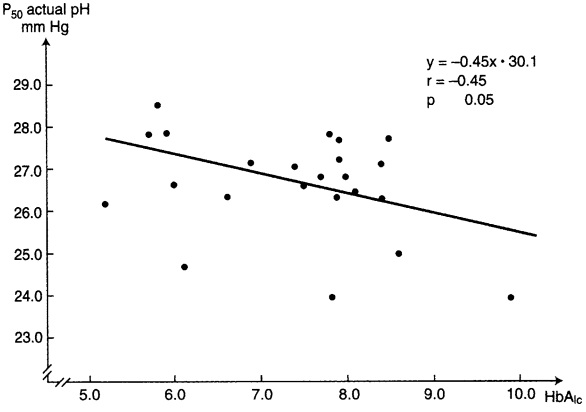

Figure 14–1. Correlation between HbA_{1c} and P_{50} at actual pH in diabetic women. (Adapted from Madsen and Ditzel.[2])

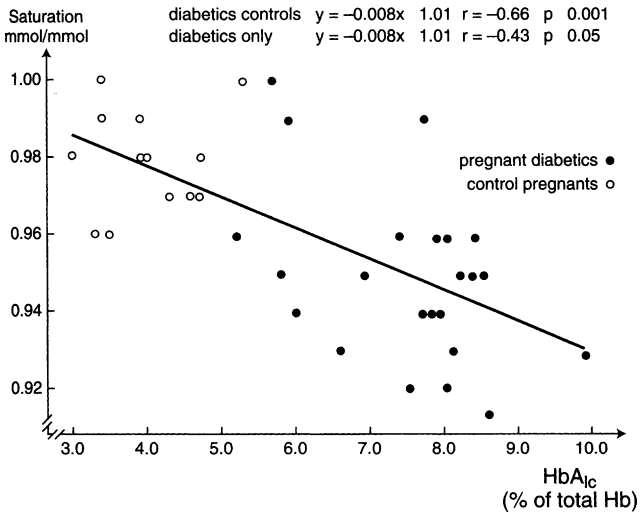

Figure 14–2. Correlation between HbA_{1c} and arterial oxygen saturation in diabetic women. (Adapted from Pian-Smith et al.[59])

Deranged Buffering Capacity in Infants of Diabetic Mothers. Broulliard et al. observed an interesting phenomenon suggesting that infants of diabetic mothers have a decreased buffering capacity and a different response to an increased acid load. There is an increased affinity of hemoglobin to oxygen in infants of diabetic mothers. The P_{50} (torr) values were significantly less in infants of diabetic mothers when compared with control infants (17.9 vs. 22.6).[3] This multiplicity of problems makes infants of diabetic mothers more vulnerable to hypoxia.

Placental Transfer of Insulin. It has been shown that insulin could cross the placenta from the maternal to the fetal circulation as insulin–anti-insulin antibody complexes.[4] This must be taken into consideration in the management of blood sugars in the diabetic parturients.

Anesthetic Management

Labor and Delivery. For labor and vaginal delivery moderate pain relief can be obtained by administering small doses of narcotics early in the first stage. A lumbar epidural block can provide excellent pain relief for both labor and delivery. It has been noted that the fetus entered the second stage in a less acidotic state when mothers received epidural analgesia compared to fetuses whose mothers did not receive any analgesia.[5] The acidosis was metabolic in origin and was related to high lactate concentrations. One report suggested that epidural analgesia will reduce the level of maternal endogenous catecholamines during labor, and this might benefit placental perfusion, a factor possibly more important in this particular group of parturients.[6]

Spinal anesthesia (bupivacaine 2.5–3 mg, fentanyl 25–30 μg) can also be used if required at the time of delivery. *One should use a separate intravenous line for the rapid infusion of non-dextrose-containing solutions if necessary to treat hypotension without producing hyperglycemia.* It is also important to realize that the fetus of a diabetic mother might be quite susceptible to hypoxia secondary to maternal hypotension.

Anesthesia for Cesarean Section. The incidence of cardiovascular depression is higher during regional anesthesia for cesarean section and is related to a higher sympathetic blockade accentuated by compression of the inferior vena cava and aorta by the gravid uterus.

Datta et al. compared spinal and general anesthesia for abdominal delivery in healthy mothers and diabetic parturients. They found that infants of diabetic mothers receiving spinal anesthesia were more acidotic than infants of diabetic mothers receiving general anesthesia.[7] The acidosis appeared to be related to both maternal diabetes and maternal hypotension. Subsequently, maternal and neonatal acid–base values were also examined by Datta et al. after administering epidural anesthesia.[8] They observed a 60% incidence of neonatal acidosis (umbilical artery pH of 7.20 or less) during epidural anesthesia.[8] The fetal acidosis was related to both the degree and the presence of maternal hypotension. The umbilical artery pH was always greater than 7.20 in the absence of maternal

Table 14–1. Effect of Hypotension in Infants of Diabetic Mothers Following Spinal or Epidural Anesthesia for Cesarean Section

Anesthesia	No Hypotension	Hypotension
Spinal anesthesia ($N = 15$)		
Umbilical artery pH	$7.24 \pm 0.0_2$[†]	7.16 ± 0.01[‡]
PO_2 (mmHg)	19 ± 2	16 ± 2
PCO_2 (mmHg)	65 ± 3	71 ± 4[‡]
Base deficit (mEq/L)	4.35 ± 0.88	8.25 ± 1.74[‡]
	$n = 9$	$n = 6$
Epidural anesthesia ($N = 16$)		
Umbilical artery pH	7.26 ± 0.02	7.16 ± 0.01[‡]
PO_2 (mmHg)	25 ± 2.5	18 ± 1.3[‡]
PCO_2 (mmHg)	52 ± 2	65 ± 3[†]
Base deficit (mEq/L)	5 ± 1.2	10 ± 0.6[‡]
	$n = 6$	$n = 10$

[†]Mean ± SE.
[‡]*p*, 0.05.
Data from Datta and Brown[7]; and Datta et al.[8]

hypotension (Table 14-1). Datta et al. used 5% dextrose with lactated Ringer's solution for acute volume expansion in both studies.

The genesis of the fetal acidosis in pregnant diabetic parturients appears to be complex, and several factors might be involved: (1) the human placenta produces lactate in vitro, especially under conditions of hypoxia or increased glycogen deposition as in maternal diabetes, (2) fetal lactic acidemia might occur due to hypoxia (secondary to maternal hypotension) in the presence of hyperglycemia following acute volume loading with dextrose-containing solutions. An additional risk of maternal and fetal hyperglycemia accompanying acute volume expansion with dextrose-containing solutions before cesarean section in diabetic parturients is the occurrence of neonatal hypoglycemia. (3) Finally, it has been observed that chronic infusion of insulin directly into the sheep fetus increased fetal glucose uptake, increased oxidative utilization of glucose by the fetus, and surprisingly, reduced the fetal arterial oxygen content.[9] Hyperinsulinemia may increase oxygen consumption. Fetal hyperglycemia and hyperinsulinemia might

result in reduced fetal oxygenation in pregnancies complicated by uncontrolled diabetes (Fig. 14-3).

In another study, Datta et al. re-evaluated the acid–base status (Table 14-2) of ten rigidly controlled insulin-dependent diabetic mothers and ten healthy nondiabetic control women having spinal anesthesia for cesarean section.[10] The parturients were all well controlled, dextrose-free intravenous solutions were used for volume expansion before induction of anesthesia, and hypotension was prevented in all cases by prompt treatment with ephedrine. There were no significant differences in the acid–base values between the diabetic and nondiabetic mothers and the infants of the diabetic and control groups. Datta et al. concluded that (1) if maternal diabetes is well controlled, (2) if dextrose-containing solutions are not used for maternal intravascular volume expansion before delivery, and (3) if maternal hypotension is avoided, regional anesthesia can be used safely for diabetic mothers having cesarean section. If general anesthesia is used, metoclopramide should be used preoperatively because the incidence of gastric stasis may be high in this group of women. Finally, one should also remember the significant decrease in insulin requirement immediately after delivery.[11] *Impaired counterregulatory hormone responses to hypoglycemia during sleep have been also observed in diabetic subjects.*[12] Although no clinical study exists, one should speculate that the IDDM parturients may benefit from cesarean section under regional rather than general anesthesia due to less catecholamine surge during regional anesthesia as compared to general anesthesia.

In summary, the key points of anesthesia for cesarean section diabetic parturients are

1. Hydration using non-dextrose-containing solutions (separate intravenous line if necessary).
2. Routine left uterine displacement is used.
3. Hypotension is promptly treated with intravenous ephedrine.
4. A well-conducted general anesthesia can be used if necessary with good neonatal outcome.

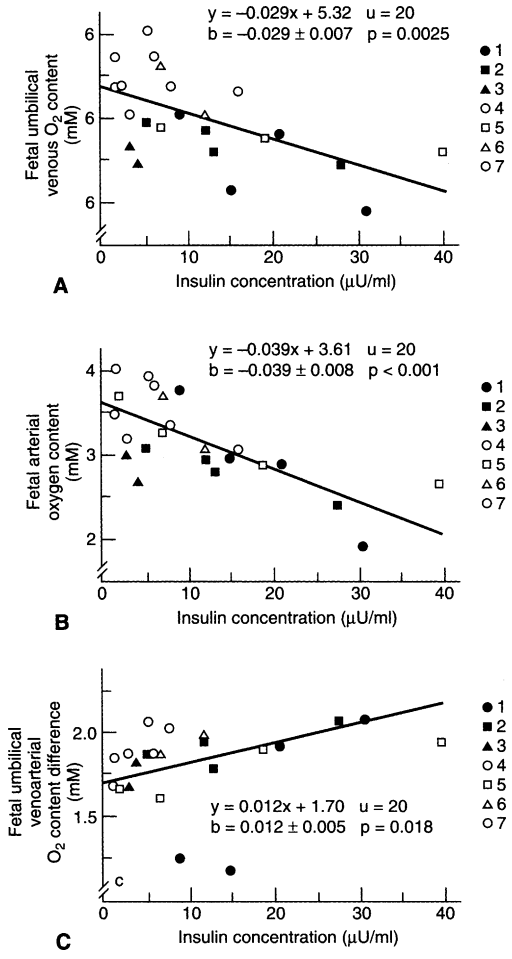

Figure 14–3. Relationship between fetal plasma insulin concentration and (**a**) fetal arterial oxygen content, (**b**) fetal venous oxygen content, and (**c**) fetal umbilical venoarterial oxygen content difference. (From Milley et al.[9] Used with permission from Elsevier.)

Table 14–2. Acid–Base Values in Infants of Diabetic Mothers with Rigid Glucose Control, Non-Dextrose-Containing Solution for Volume Expansion, and Prevention of Maternal Hypotension

Umbilical Artery ($n = 20$)	No Hypotension (Diabetic) ($n = 10$)	No Hypotension (Control) ($n = 10$)
pH	7.27 ± 0.01[†]	7.30 ± 0.01
PO_2 (mmHg)	20 ± 2	22 ± 2
PCO_2 (mmHg)	56 ± 2	50 ± 2.5
Base deficit (mEq/L)	4 ± 1	3 ± 0.7

[†]Values represent mean ± SE.
From Datta et al.[10] Used by permission.

Hyperthyroidism

Major problems involving parturients with hyperthyroidism include the following:

1. The parturient might be receiving propranolol therapy.
2. If the mother is receiving antithyroid therapy, fetal goiter may occur.
3. The myocardium remains hypersensitive to catecholamines in such cases.
4. There is a possibility of thyroid storm. Thyroid storm, an exaggerated hypermetabolic state of thyrotoxicosis, is rare during pregnancy. Clinical signs include high fever, tachycardia, agitation, and severe dehydration. The important differential diagnosis is malignant hyperthermia.

Anesthetic Management

Regional anesthesia, especially spinal anesthesia, may be avoided, especially for cesarean delivery, if the mother is taking high doses of propranolol due to exaggerated post-spinal hypotension. Epidural anesthesia is a reasonable alternative to spinal anesthesia.

Pheochromocytoma

During pregnancy this entity carries high maternal and fetal mortality rates. Although epidural anesthesia can be used for labor and delivery, for cesarean section, an epidural or continuous spinal and general anesthesia may be used. Prior treatment with α- followed by β-adrenergic blockers is indicated in elective cesarean section. Cases have been reported in which cesarean section was successfully performed under epidural analgesia in patients whose pregnancy was complicated by a pheochromocytoma. Pre-operative phenoxybenzamine therapy together with careful peri-operative monitoring produced cardiovascular stability.[13] Occasionally, pheochromocytoma can mimic preeclampsia in pregnancy.[14] Pheochromocytoma has been successfully removed during cesarean section after the delivery of the baby under combined regional and general anesthesia.[15,16]

Cardiac Disease

Rheumatic fever-related acquired heart problems have decreased dramatically in recent years, and with better surgical technique, the future population will become pregnant with fewer congenital cardiac problems. However, the surgical corrective procedures performed pose a new challenge for obstetric anesthesiologists as they are required to understand the altered anatomical and physiological cardiovascular flow dynamics that have enabled the women to reach pregnancy state. The incidence of heart disease during pregnancy varies from 0.4% to 4.1%. Major cardiac problems can be divided into acquired, congenital, and surgically altered anatomical and physiological functions during corrective surgery for congenital lesions:

I. *Acquired* cardiac disease
   A. Mitral stenosis
   B. Mitral insufficiency
   C. Mitral valve prolapse
   D. Aortic stenosis
   E. Aortic insufficiency

II. *Congenital* cardiac disease
   A. Left-to-right shunt
      1. Ventricular septal defect
      2. Atrial septal defect
      3. Patent ductus arteriosus
   B. Right-to-left shunt
      1. Tetralogy of Fallot
      2. Eisenmenger's syndrome
   C. Corrective surgical procedures altering anatomical and physiological function.

Patients with cardiac disease can be affected by some of the important physiological changes during pregnancy as well as during labor and delivery. An increase in cardiac output is the most important physiological change. *Cardiac output maximally increases during pregnancy at 28–32 weeks of gestation, and labor and delivery can impose further stress. During the first stage of labor, cardiac output increases 15–30% because of autotransfusion (300–500 mL) during each uterine contraction, and due to increases in the heart rate due to the effect of catecholamines. During the second stage, cardiac output can increase further, and the highest cardiac output is observed immediately after delivery due to autotransfusion (potentially up to 80% above normal)* (Fig. 14-4).

Some of the patients may be on anticoagulants for preventing thromboembolic phenomena. *Heparin is usually the drug of choice (does not cross placenta),* but oral anticoagulant therapy should be discontinued before the time of delivery to avoid potential fetal bleeding caused by the trauma of delivery. Parturients with cardiac lesions can be also receiving beta-blockers, digoxin, diuretics, etc.

Anesthetic Management

It is wiser to have the cardiologist monitor the cardiovascular status of pregnant women during the course of pregnancy and appropriate adjustments made in the therapeutic medications. Heparin treatment should be stopped before induction of labor or elective cesarean section, and the aPTT should be measured if regional analgesia/anesthesia is to be used.

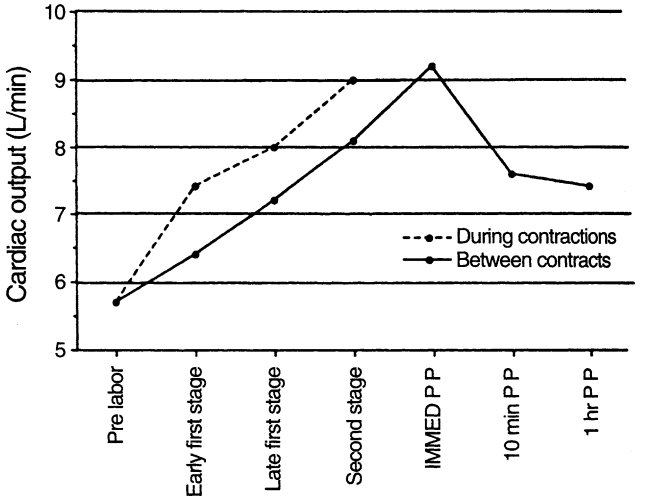

Figure 14–4. Changes in cardiac output during the first and second stages of labor. (From Datta.[60] Used with permission from Elsevier.)

Anesthetic management of cardiac disease in pregnancy can be summarized as shown in the outline below.

I. Acquired heart diseases:
   A. Labor and delivery:
      1. Relief of stress and apprehension should be accomplished during labor by the administration of tranquilizers.
      2. For relief of pain, epidural analgesia should be considered.
      3. Hypotension should be avoided by carefully administering fractionated doses of epidural local anesthetics. Aortocaval compression should be avoided. If there is hypotension, *phenylephrine in dilute solution is preferable to ephedrine because ephedrine can increase the heart rate, which is not preferable in stenotic lesions. Fractionated boluses of intravenous fluids may be required to maintain adequate preload during enhancement of epidural blockade.*

B. Cesarean section:
   1. Parturients with aortic insufficiency and mitral insufficiency can tolerate epidural anesthesia or the continuous spinal technique.
   2. Pregnant women with severe aortic stenosis or mitral stenosis need close and careful attention. Both regional anesthesia (epidural) and general anesthesia have been used. If general anesthesia is selected, then a high-dose narcotic technique is preferable.
   3. Depending upon the cardiovascular functional status, an arterial line to monitor blood pressure is a reasonable option. Occasionally, central line and PA catheters may be needed in a small subset of patients with either ventricular failure or pulmonary hypertension. Insertion of PA catheters has been a rarity in our institution where we provide care to several parturients with cardiac lesions. The functional status of the patient dictates the modus operandi rather than the anatomical lesions.

II. Congenital heart lesions:
   A. Labor and delivery:
      1. *Hypotension will reverse the left-to-right shunt. For this reason, high sympathetic block should always be avoided.*
      2. Epidural analgesia with proper invasive monitoring can be used for labor and delivery. This will be beneficial for complete relief of pain and abolition of bearing down, which might further increase the right atrial, right ventricular, and pulmonary pressures. Hypotension should be treated with small doses of phenylephrine. Recently, intrathecal narcotics have been used for maintaining cardiovascular stability.
      3. A combination of systemic analgesics and tranquilizers during the early first stage with a paracervical block during the active phase and a bilateral pudendal block during delivery can also be used. *One must be aware of the problems associated with paracervical blocks, and continuous fetal monitoring is mandatory.*

4. Regional anesthesia is contraindicated if anticoagulant treatment must be continued for any reason.

B. Cesarean section:
   1. Epidural anesthesia has been used with invasive monitoring; postoperative analgesia can be used by the epidural route.
   2. General anesthesia can be used with the high-dose narcotic technique. The newborn can be resuscitated appropriately.
   3. A dilute oxytocin solution should be infused to prevent postpartum uterine relaxation and excessive blood loss. A *bolus intravenous injection of oxytocin may cause serious hypotension, while intramuscular ergonovine preparations may produce severe peripheral vasoconstriction followed by hypertension. Both these drugs should be used carefully during cesarean delivery. In patients, where optimum fluid balance was achieved prior to labor and delivery by diuretics, further use of postpartum diuretics should be considered.*
   4. Parturients receiving propranolol are always at "greater risk" because anesthesiologists may face problems related to a reduction in cardiac output and maternal myocardial reserve, as well as decreased responsiveness to β-adrenergic-stimulating drugs in the presence of hypotension. Parturients receiving high doses of propranolol may not be candidates for major regional anesthesia for cesarean delivery. Despite this concern, a carefully administered epidural anesthesia is an option that can avoid general anesthetic. *The effects of the chronic administration of propranolol on the fetus include intrauterine growth retardation, fetal bradycardia, and neonatal hypoglycemia, so babies need careful postpartum attention in such cases.*

III. Surgical procedures altering anatomical and physiological function: Congenitally corrected transposition of the great arteries (CCTGA) is an uncommon congenital heart disease characterized by inversion of the ventricles resulting in

both atrioventricular (AV) and ventricular-great artery discordance. As a consequence, deoxygenated blood flows from the right atrium, through the left ventricle, and into the pulmonary artery (PA). In contrast, oxygenated blood flows from the left atrium, through the right ventricle, and into the aorta. Because the morphologic right ventricle and tricuspid valve are in the systemic circulation, most patients will develop systemic (morphologic right) ventricular dysfunction and varying degrees of systemic AV (morphologic tricuspid) valve regurgitation with increasing age. Similarly, the hemodynamic stress of pregnancy, labor, and delivery may also lead to ventricular failure and valvular dysfunction.[17]

The cases of this type have been well managed with right radial arterial line and epidural anesthesia. Anesthesia was gradually achieved via incremental doses of bupivacaine with fentanyl.[17] Varieties of shunting procedures are being performed in infants with cardiac anomalies. It is essential to understand the physiology of cardiovascular function in these individuals. A management strategy has to be evolved in conjunction with cardiologists. The vast experience at Brigham and Women's Hospital demonstrates that the pregnant patients with shunting procedures do well with epidural anesthesia during labor and delivery.

The anesthetic management for cardiac disease can be summarized as follows:

A. The pregnant woman should be consulted at 24–32 weeks' gestation because cardiac output is highest at this stage. The parturients can be classified into four groups according to New York Heart Association classification (Table 14-3).
B. Depending on the NYHA classification, one can decide the monitoring of the parturients:
    a. Invasive monitoring should include arterial line, CVP line with cordis, and PA catheter in rare cases.
C. Anesthetic management for labor and delivery may include early epidural analgesia. Sensory analgesia levels should be increased gradually, observing the mean arterial pressure and CVP, if present. A decrease in blood pressure should be treated with a judicious volume of fluid and vasopressors.

Table 14–3. New York Heart Association Functional Classification

Class I	Asymptomatic
Class II	Symptomatic with exertion
Class III	Symptomatic with normal activities
Class IV	Symptomatic at rest

Phenylephrine in small doses (50–100 μg) should be used unless contraindicated, in which case ephedrine may be the drug of choice. Sensory levels should be maintained to T_6. For the second stage perineal anesthesia should be dense (cardiac delivery) to prevent the urge to push. Forceps or vacuum extraction is usually performed. If emergency cesarean section is necessary, the surgical anesthesia can be obtained using either with 2% plain lidocaine (lidocaine with epinephrine as the case may be) 0.5% ropivacaine or 0.5 bupivacaine mixed with opioids (fentanyl or sufentanil). If general anesthesia is deemed necessary, induction of anesthesia with opioids, or mixed with etomidate, will be the ideal choice. Remifentanil has been used recently for cesarean section in parturients with cardiac anomalies.[18–20] A single bolus of 1 μg/kg remifentanil effectively attenuated hemodynamic changes after induction and tracheal intubation. However, remifentanil crosses the placenta and may cause mild neonatal depression and thus should be used for definitive maternal indication and when adequate facilities for neonatal resuscitation are available.

Respiratory Problems

Bronchial Asthma

Bronchial asthma might be expected to improve during pregnancy due to the bronchiolar relaxing effect of progesterone. However, it has been shown that pregnancy has no consistent effect on the course of asthma. Medical therapy is the same as in nonpregnant women. For labor and delivery, one should use a continuous epidural block.

Cesarean Section

The possibility of drug interactions should be borne in mind when taking care of pregnant women with a history of bronchial asthma. Different medications that have been used are (1) methylxanthines, e.g., theophylline, aminophylline; (2) β-mimetic drugs, e.g., metaproterenol, albuterol (salbutamol), terbutaline, inhaled β-mimetic agonists (the primary medications for the treatment of acute asthma at the present time); and (3) corticosteroids.

Regional Anesthesia

Studies have suggested that although regional anesthesia has minor effects on inspiratory effort,[21] its effect on expiratory function can be significant. *Spinal anesthesia, because of its more intense motor block, can affect abdominal muscle function as well as cough strength, thus affecting expiratory function considerably.* Severe bronchoconstriction following spinal anesthesia in a parturient with severe asthma has been reported.[22] The author suggested that diminished epinephrine secretion from the adrenal medulla because of sympathectomy might have triggered the bronchospasm. Epidural anesthesia is preferred over spinal anesthesia as the regional anesthetic of choice in a parturient with severe asthma. The gradual onset of epidural anesthesia enables the parturient to tolerate intercostal muscle weakness without resulting in panic attacks. An interesting study observed less dense intercostal motor block with 0.5% bupivacaine compared to 2% lidocaine with epinephrine (this should be true for 0.5% ropivacaine).[23]

General Anesthesia

General anesthesia should be avoided in parturients with respiratory problems if possible because the endotracheal tube can trigger severe bronchospasm. However, if it is absolutely essential, several precautions involving premedication should be taken: (1) H2-receptor blockers like cimetidine and ranitidine should be avoided because the H2-receptor blockade

can increase the sensitivity to histamine-induced bronchoconstriction;[24] (2) a nonparticulate antacid, 0.3 M sodium citrate, 30 mL, should be used routinely; and (3) atropine and glycopyrrolate can reduce oral secretions and will also cause bronchodilatation; hence some anesthesiologists will use these drugs as a premedicant. *However, these drugs can reduce gastroesophageal sphincter tone.*

Induction Agents. Ketamine should be the drug of choice (in the presence of bronchoconstriction) because it can relax the bronchial muscles through central catecholamine release (Fig. 14-5). Succinylcholine can be used for intubation. Of the nondepolarizing muscle relaxants, vecuronium and cisatracurium are good alternatives.

Most of the inhalational agents provide bronchodilatation. *Ventricular tachycardia and arrhythmias can occur if halothane is used in the presence of aminophylline or β-mimetic drugs. But halothane is seldom used presently.* Recently sevoflurane has been suggested as an alternative to halothane and isoflurane, as it has minimal respiratory stimulating effect unlike desflurane. *Inhalation anesthetics can cause uterine muscle relaxation and predispose to obstetric hemorrhage. Intraoperative bronchoconstriction can be effectively treated with β-mimetic drugs administered from a metered-dose inhaler.* Extubation also needs careful attention.

Cystic Fibrosis

Pregnant women with cystic fibrosis should be followed closely with respect to their lung function. These parturients are often associated with severe pulmonary obstruction and respiratory impairment. *For labor and delivery, epidural analgesia is usually the best choice.* For cesarean section, the anesthetic technique will depend on the condition of the pregnant woman. Epidural anesthesia should be used whenever possible. This technique is associated with fewer pulmonary complications and can also be utilized for excellent postoperative pain relief. Parturients with severe respiratory impairment may need general anesthesia.

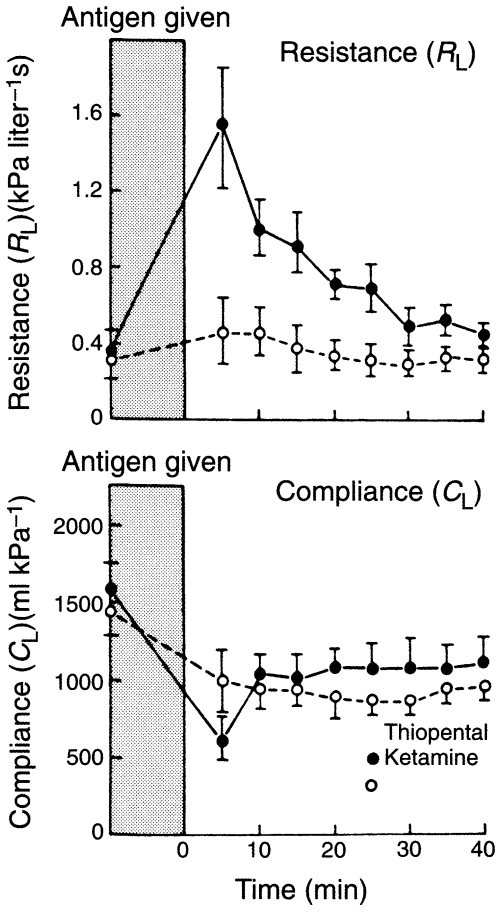

Figure 14–5. Changes in pulmonary resistance in sensitized dogs anesthetized with ketamine or thiopental. (From Hirshman et al.[61] Used with permission.)

Neurological Problems

Neurological problems are uncommon during the childbearing age. Regional anesthesia is contraindicated in the presence of active inflammatory disease in the spinal canal, acute

meningitis, or superficial infection at the site of the lumbar puncture. However, regional anesthesia may not be contraindicated in old inflammatory problems, e.g., a parturient with a history of poliomyelitis.

Paraplegia

The unique phenomenon experienced by paraplegics and quadraplegics is called autonomic hyperflexia or mass reflex. Interestingly, the syndrome is not found if the lesion is below T7. It occurs in 85% of cases with lesions above T7 (Fig. 14-6).

Stimulation of the skin below the level of the lesion, the presence of distension, or contraction of a hollow viscus like urinary bladder, uterus, or gut might precipitate the mass reflex.

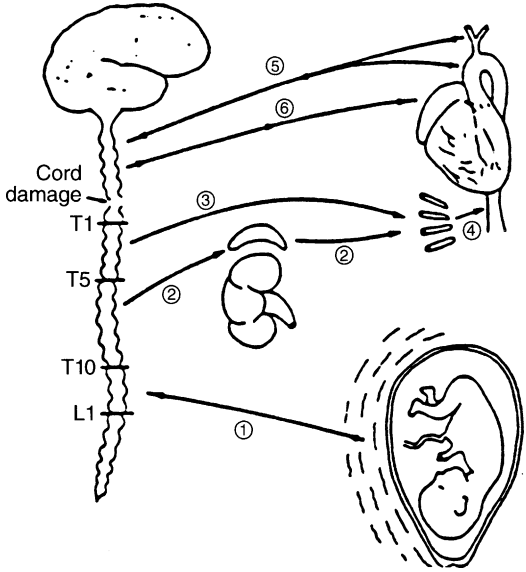

Figure 14–6. Mechanism of autonomic hyperreflexia in paraplegic and quadriplegic patients. (From Abouleish et al.[62] Used with permission.)

This might present in the form of pilomotor erection, sweating, facial flushing, severe headache, bradycardia, and severe hypertension leading to convulsions, loss of consciousness, and possible subarachnoid or cerebral hemorrhage. Eleven percent of paraplegic patients may develop severe hypertension during pregnancy due to mass reflex. The incidence of premature labor is high among paraplegics.

Anesthetic Management

Labor and Delivery. Epidural analgesia should be used as soon as the patient goes into labor to prevent autonomic hyperreflexia and mass reflex. At Brigham and Women's Hospital, continuous epidural infusion with 0.125% bupivacaine and 2 μg fentanyl per milliliter (10 mL/h) has been used with excellent outcome. Patient-controlled epidural anesthesia (PCEA) is an also a good option. Epidural meperidine has been used in one case with success.[25] The main advantage of epidural opioids is sparing of the resting sympathetic tone, which may already be impaired following cord transection.

Cesarean Section. Epidural anesthesia is preferable to spinal anesthesia because the chances of hypotension are less. If general anesthesia is essential, one should avoid succinylcholine administration because of the possibility of hyperkalemia.

Cerebrovascular Accidents

Arterial or venous thrombosis is not common. Cerebral hemorrhage can be seen in association with severe preeclampsia. Subarachnoid hemorrhage can occur during pregnancy due to a leaking aneurysm or arteriovenous malformation. Cardiovascular stresses during pregnancy, labor, delivery, and the immediate postpartum period can precipitate a subarachnoid hemorrhage.

Anesthetic Management

For labor and delivery a continuous epidural block is advisable. The use of forceps is indicated to shorten the second

stage. In the immediate postpartum period, one should be prepared to treat hypertension aggressively if it occurs. For cesarean delivery, an epidural block is the anesthesia of choice; however, if there is fetal distress or if general anesthesia is indicated for some other reason, one has to be careful about the hypertensive response following endotracheal intubation.

Multiple Sclerosis

This disease is characterized by demyelination of the brain and spinal cord. The course is associated with remissions and exacerbations, and is unpredictable in nature. *However, the relapse rate during the first 3 months postpartum is known to be about three times higher than that in nonpregnant individuals.*[26]

Anesthetic Management

Bader and colleagues observed the relationship of anesthetic techniques and the type and amount of anesthetic agent used with the postpartum relapse rate of multiple sclerosis at Brigham and Women's Hospital between 1982 and 1987.[27] Postpartum relapses occurred in 9 of the 32 pregnancies during the first 3 months. Seven women had vaginal delivery, whereas two parturients underwent cesarean section (Tables 14-4, 14-5 and 14-6). Pregnant women who had epidural anesthesia for vaginal delivery did not have a significantly

Table 14–4. Relapse Rate of Multiple Sclerosis in the First 3 Months Postpartum

Type of Anesthetic	Cesarean Delivery (No. of Cases)	Relapse No.
Epidural	5	1
General	3	1
	Vaginal Delivery	
Epidural	9	4
Local	13	2
General	2	1

From Bader et al.[27] Used with permission from Elsevier.

Table 14–5. Epidural Local Anesthetics Used for Vaginal Delivery in Patients with Multiple Sclerosis

Drug	No. of Cases	Relapse No.
Bupivacaine, 0.25%	4	0
Bupivacaine, 0.5%	2	2
Bupivacaine, 0.5%, + lidocaine, 2%	1	1
Lidocaine, 2%	1	0
Drugs unknown	1	0

From Bader et al.[27] Used with permission from Elsevier.

Table 14–6. Local Anesthetics Used for Cesarean Section

Drugs Used	No. of Cases	Relapse No.	Indication
Lidocaine, 2%	2	0	Breech, previa
Lidocaine, 2%, + bupivacaine, 0.5%	1	0	Previa
Bupivacaine, 0.5%, + chloroprocaine, 3%	1	0	Fetal distress
Bupivacaine, 0.5%, + lidocaine, 2%, + chloroprocaine, 3%	1	1	Failure to progress

From Bader et al.[27] Used with permission from Elsevier.

higher incidence of postpartum relapse than did parturients who received either pudendal or local infiltration. Interestingly, in the relapsed population, all women received a higher concentration of local anesthetic for a prolonged period (>0.25% bupivacaine). The authors suggested (1) that there is no absolute contraindication to the use of regional analgesia for labor and delivery, (2) that the parturient should be informed beforehand about the possibility of postpartum relapse not related to anesthesia, and (3) that lower concentrations of local anesthetics should be used in these individuals to minimize the concentration of anesthetic that reaches the spinal cord.

Space-Occupying Lesions (Brain Tumors)

Labor and Delivery

Spinal anesthesia may be relatively contraindicated in brain tumors because of a sudden reduction in cerebrospinal fluid (CSF) pressure; if it occurs rapidly, it may produce cerebral herniation and death. *On the other hand, painful uterine contractions and bearing-down efforts during labor will increase intracranial pressure; hence epidural analgesia may be indicated, but one should bear in mind the consequences of accidental dural puncture.* Some authors suggest the use of a bilateral lumbar sympathetic block for the first stage of labor and a pudendal block for the second stage.

Cesarean Section

Most anesthesiologists prefer to use general anesthesia for this purpose. Nonetheless, epidural anesthesia is an option to be considered. For general anesthesia, induction with *large doses of narcotics, hypotensive medication (if necessary), sodium thiopental (Pentothal), succinylcholine, and vecuronium* may be used. *Isoflurane is the inhalation anesthetic of choice since it does not increase cerebral blood flow.*[28] *Although hyperventilation can reduce the intracranial pressure, it can affect the uteroplacental circulation, and continuous fetal heart rate monitoring, if possible, may be useful until delivery.* Arterial and CVP lines may be indicated based on the circumstances. Depending upon the severity of the increase in intracranial pressure, neurosurgeons may prefer to reduce the intracranial pressure by surgical drainage before cesarean section. *Medical therapy to decrease intracranial pressure includes* steroids and diuretics like furosemide or mannitol, which obviously will be used before surgical intervention. A close FHR monitoring is necessary while using mannitol because of the possibility of severe maternal and fetal hypovolemia. Reduced uteroplacental circulation is also a possibility. Constant communication is necessary between the neurologist, neurosurgeon, obstetrician, and anesthesiologist.

In benign intracranial hypertension (pseudotumor cerebri), *the increased intracranial pressure is not related to intracranial*

mass, infection, or obstruction to CSF outflow and may be related to decreased CSF absorption. Regional anesthesia, spinal or epidural, is preferred for both vaginal delivery and cesarean section.

Epilepsy

There is no evidence that epileptic groups are more susceptible to convulsion from local anesthetics than the normal population. *Spinal or epidural anesthesia is not contraindicated in such cases. For general anesthesia, drugs that have potential convulsive action, e.g., enflurane or ketamine, should be avoided.*

Myasthenia Gravis

The major problems encountered in parturients with myasthenia gravis are as follows:

1. Chance of a prolonged second stage of labor because of muscle weakness
2. Postdelivery pulmonary complications because of respiratory muscle weakness
3. Complications during anesthesia
4. Possibility of neonatal myasthenia gravis

Myasthenic or cholinergic crisis may be evident by progressive generalized bulbar and respiratory weakness. Occasionally, differential diagnosis may be difficult:

Myasthenic crisis	*Cholinergic crisis*
Progressive deteriorization of the disease process evidenced by cranial nerve involvement (ocular symptoms) as well as respiratory muscle weakness	Often associated with high doses of antiacetylcholinesterase therapy and accompanied by muscarinic side effects like diarrhea, sweating, abdominal muscle cramps, fasciculations, palpitations, increased secretions, and bradycardia.

When differentiation between the cholinergic and myasthenic crisis is not definitive, parturients occasionally may need ventilation and supplemental feeding. Antiacetylcholinesterase should be stopped and then gradually restarted in case of cholinergic crisis. In myasthenic crisis, women may need plasmapheresis followed by immunosuppressive therapy. Although rare, myasthenic parturients may be associated with pregnancy-induced hypertension (PIH). Use of magnesium sulfate for PIH is contraindicated in this situation. Phenytoin may be used in these cases.[29]

Labor and Delivery

Epidural anesthesia is a good option for these patients for labor and delivery analgesia.

Cesarean Delivery

Because of the need of a higher level of sensory anesthesia for cesarean delivery, there is always a danger of impairment of the respiratory and swallowing muscles following regional anesthesia. Unless contraindicated because of respiratory insufficiency, regional anesthesia should be the technique of choice. Epidural anesthesia may have distinct advantage as the level of anesthesia can be brought upwards slowly so that the patient has the opportunity to get used to breathing without the assistance of abdominal muscles. Spinal anesthesia has also been used for cesarean delivery successfully. The advantages of neuraxial anesthesia include avoidance of IV opioids, neuromuscular blocking drugs, and anticholinesterases. For epidural, amide *local anesthetics are preferable to esters because the women are usually receiving anticholinesterase drugs for their treatment and these can prolong ester local anesthetic activity.*[30–32] *Occasionally, patients may need respiratory assistance via BIPAP during regional anesthesia.*[31]

In cases where general anesthesia is indicated, the principles guiding anesthetic management of patients with myasthenia gravis in pregnancy are similar to those used in nonpregnant patients. Due to acetylcholine receptor down-regulation,

patients are very sensitive to nondepolarizing muscle relaxants and potentially resistant to depolarizing muscle relaxants. However, the effect of depolarizing muscle relaxants has been described as inconsistent in patients with myasthenia gravis.[33] Depolarizing muscle relaxant activity can be prolonged in the presence of anticholinesterase therapy. Despite this succinylcholine should be used to facilitate intubation.. Nondepolarizing muscle relaxants should be used in small doses, and a neuromuscular blockade monitor must be used. The anesthesia can be supplemented with short-acting opioids, muscle relaxants, and inhaled anesthetics. Tranquilizers and narcotics should be used cautiously because of the chance of respiratory depression postoperatively.

Neonatal Myasthenia Gravis

A transient form of myasthenia gravis occurs in 12% of babies born to myasthenic mothers. It develops within the first 4 days of life. Symptoms include lethargy, poor sucking reflex, feeble cry, generalized muscle weakness, or absent or weak Moro's reflex. Diagnosis is confirmed by using edrophonium chloride, 0.05–0.1 mL, subcutaneously.

Anticholinesterase therapy may be necessary up to 4 weeks.

Renal Disorders

Physiological Changes

The major physiological changes are as follows:

1. *The effective renal plasma flow and glomerular filtration rate (GFR) increase by 50% by 16 weeks' gestation.*
2. The high renal plasma flow and GFR result in an increase in creatinine clearance.
3. During normal pregnancy, the blood urea nitrogen (BUN) level averages 8–9 mg/dL and creatinine, 0.46 mg/dL. *Therefore, during pregnancy, normal nonpregnant BUN (10–20 mg/dL) and creatinine (0.5–1.2 mg/dL) levels may represent renal compromise.*
4. One of the most common disorders in pregnancy that involves kidney function is preeclampsia.

5. Acute renal failure in pregnancy can occur in conjunction with hemorrhage, sepsis, or preeclampsia.

Anesthetic Management

Several important factors have to be considered before the anesthetic technique is selected:

1. The parturients should undergo dialysis before surgery if time permits.
2. Arteriovenous fistulas should be carefully protected during surgery.
3. *Because of the presence of anemia, hyperventilation should be prevented because this will shift the O_2 dissociation curve to the left.*
4. Drug interactions:
   - Abnormal protein binding may cause prolongation of the thiopental effect.
   - Non depolarizing muscle relaxants dependent on renal clearance should not be used because they are excreted mainly by the kidney: Pancuronium, and to some extent vecuronium, excretion can be prolonged in the presence of renal failure, and cisatracurium is a good choice in these patients.
   - Succinylcholine can increase serum potassium levels; hence, they should be contraindicated in parturients with hyperkalemia. However, patients with chronic renal failure may be more tolerant of hyperkalemia.

Labor and Delivery

Epidural analgesia should be the technique of choice.

Cesarean Section

Epidural technique is preferred over spinal because of less chance of severe hypotension and less need of volume loading, which might be detrimental in parturients with chronic renal failure. If general anesthesia is deemed necessary, the use of succinylcholine depends on potassium level, and if the patient is undergoing frequent dialysis. Propofol, remifentanil,

and ketamine combination can be used with cisatracurium as neuromuscular blocker of choice. Isoflurane and desflurane are the inhalation anesthetics of choice.

Hematological Disorders

Besides the hereditary clotting defects, the defects that are of concern in obstetric population are the acquired problems[34]:

1. Drugs that interfere with platelet function (e.g., aspirin, NSAIDS).
2. Massive transfusion of old bank blood.
3. Liver failure.
4. Disseminated intravascular coagulation, associated with abruptio placentae, amniotic fluid embolism, intrauterine fetal death, and severe preeclampsia. The pathophysiology of disseminated intravascular coagulation consists of simultaneous uncontrolled activation of procoagulants and fibrinolytic enzymes in the microvasculature. The process depletes platelets and procoagulants. Firbrinolysin (plasmin) levels are elevated and this leads to further digestion of fibrin clots, which releases fibrin degradation products and inhibits polymerization of additional fibrin.

Key points of anesthetic management of hematological disorders are:

1. General anesthesia should be the choice because of the clotting problems unless treatment with the medications is stopped beforehand and clotting parameters revert to the normal range (Fig. 14-7).
2. Blood volume replacement and circulatory support may be necessary.
3. Fresh whole blood or red cells and fresh frozen plasma containing all known clotting factors should be used. A 250-mL unit of fresh frozen plasma contains 200–400 mg of fibrinogen and also factors VIII, V, and XIII. Cryoprecipitate is a concentrated preparation of fibrinogen and contains 200–400 mg of fibrinogen in 15–20 mL. Fibrinogen concentrates have recently become available in the US.
4. The administration of procoagulants to replace factors that have been consumed is essential.

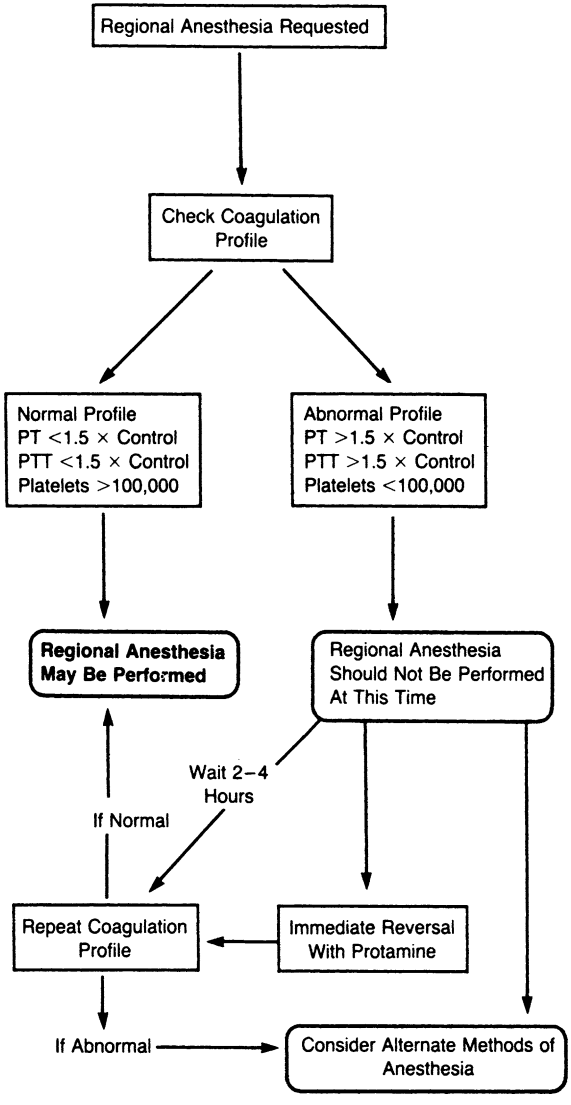

Figure 14–7. Regional anesthesia in the heparinized parturient. (From Sharma and Leveno.[63])

Sickle Cell Disease

Parturients with sickle cell trait usually have no problems during pregnancy; however, women with S/S or S/C disease may have a higher incidence of obstetric risks. Their anemia becomes more severe during pregnancy, and the incidence of preeclampsia is increased.

Anesthetic Management

Hypoxia and hypotension must be prevented because of the increased chance of sickling. Due attention should be paid to acid–base status, hydration, and temperature monitoring during management of these patients.

Labor and Delivery. Epidural analgesia is the technique of choice, and proper volume expansion with warm fluid is important. Oxygen should be administered and aortocaval compression should be avoided. Hypotension should be immediately corrected.

Cesarean Delivery. Epidural anesthesia, if properly performed, will be associated with good maternal and neonatal outcome. It can also be used for postoperative analgesia, which might be necessary in these women because they might be receiving analgesic drugs because of sickle cell crisis. Warm fluid for volume expansion should be used, and treatment of hypotension should be immediate. If general anesthesia is indicated, adequate oxygenation, maintenance of normal acid–base status, and a warm environment are essential.

Idiopathic Thrombocytopenia

Regional anesthesia may be indicated both for labor and delivery and for cesarean section, provided that the clotting parameters are normal. If coagulation parameters are abnormal and clinical features of prolonged bleeding are present, general anesthesia will be necessary for cesarean section. Gentle intubation with a small-sized endotracheal tube is important for preventing hematoma of the vocal cords.

Von Willebrand Disease

Table 14-7 describes the classification of Von Willebrand disease.

Treatment consists of DDAVP, 0.3 mg/kg, especially in type 1. DDAVP should not be given in type 2b as it may worsen bleeding. During therapy, close monitoring of vWF levels is necessary; the parturient may develop tachyphlaxis when treatment is used for more than 48 h. The administration of neuraxial block depends on the type of the disease and coagulation profile. Neuraxial block has been successfully administered in patients with type 1.[35] The customary practice at Brigham and Women's Hospital is to administer neuraxial block after checking coagulation profile and administering DDAVP, where indicated.

Hypercoaguable States

Protein C and Protein S Deficiency, Phospholipid and Cardiolipin Antibodies

Protein C is a vitamin K-dependent hepatic protein and is converted to an active protease by thrombin. Activated protein C in conjunction with protein S proteolyses factors Va and VIIIa, which interferes with the fibrin formation. Deficiencies of protein C and S cause recurrent venous thrombosis and pulmonary embolism. Presence of phospholipid and cardiolipin antibodies also result in hypercoagulable state. Heparin therapy may be necessary during pregnancy.[34]

Factor V Leiden Mutation

Carriers of the factor V Leiden mutation have a high risk of fetal loss because of placental blood vessel thrombosis. Anticoagulant therapy is indicated from the beginning of pregnancy.[36]

Presently, these patients are generally on low molecular weight heparins (LMWH). The usual procedure is to switch LMWH to regular heparin before 38 weeks' gestation to enable administering regional anesthesia following usual guidelines

Table 14–7. Classification of Von Willebrand Disease (Incidence/1:10,000)[34]

Type	vWF:Ag	vWF:RCo	Factor VIII	vWF Multimer structure	DDAVP response	Bleeding
1	↓	↓	↓	Normal	Good	Mild–moderate
2 A	↓	↓↓	↓	Abnormal	Variable	Variable
2 B	↓ to normal	↓	↓ to normal	Abnormal	May worsen thrombocytopenia	Thrombocytopenia may worsen bleeding
2 M	↓ to normal	↓	↓ to normal	Abnormal	Variable	Variable
2 N	↓ to normal	↓ to normal	↓	Normal	Variable	Variable
3	↓↓↓ or absent	↓↓↓	↓↓↓	Normal	No response	Severe

of timing of heparin withdrawal and checking PTT.[37] An alternative is to discontinue prophylactic doses of LMWH at least 10–12 h before regional anesthetic.[38] Therapeutic doses of LMWH should be discontinued at least 24 h prior to regional anesthesia. Utilization of dilute solutions of local anesthetic with opioid mixture allows for monitoring of the parturient's neurologic status after neuraxial block. It is also recommended to wait at least 2 h after the removal of an epidural catheter before giving a dose of LMWH.[39]

The heparin test, an anti-Xa chromogenic assay that is often used to follow the activity of LMWH, takes 15 min to perform at our institution. Although the American Society of Regional Anesthesia and Pain Medicine (ASRA) guidelines do not recommend following the anti-Xa level, it is the practice of the authors to perform this test in parturients that are taking therapeutic doses (>1 mg/kg enoxaparin) of anticoagulants even if the last dose was given more than 24 h before the test. We also use this test whenever a prolonged effect of LMWH is anticipated. The target is a heparin test of less than 0.2 U/ml. A recent study demonstrated a correlation between the thromboelastogram (TEG) R-time and the heparin test.[40] In the future TEG may play a significant role in determining the patient's suitability for regional anesthesia.

Autoimmune Disease

Rheumatoid Arthritis

Women with severe rheumatoid arthritis may encounter multiple problems on the anesthesiology team:

1. Difficult intubation because of severe flexion deformity of the neck along with atlantoaxial instability[41].
2. Deformity of hip, knee, and intervertebral joints, thus making insertion of an epidural needle difficult and sometimes impossible
3. Restrictive lung disease and occasionally pleural effusion
4. Associated cardiac problems
5. Involvement of peripheral nerves with associated sensory and motor deficits

6. Effect of different medications like high-dose aspirin or nonsteroidal anti-inflammatory drugs

Anesthetic Management

If possible, epidural or continuous spinal analgesia is preferable provided that the clotting parameters are within normal limits. The main advantage of this technique is the avoidance of difficult intubation if emergency cesarean section is indicated. On the other hand, some anesthesiologists prefer to secure the airway by fiberoptic technique, if necessary, before proceeding with cesarean delivery.

Systemic Lupus Erythematosus

The major problems of this multiorgan disease include the following:

1. Cardiomyopathy, chronic hypertension, coronary artery disease, and nonspecific T-wave changes on the ECG.[42,43]
2. Higher incidence of preeclampsia.[43]
3. Pulmonary vasculitis, pulmonary infarcts.
4. Renal problems, evident by the presence of high BUN and creatinine concentrations.
5. CNS as well as peripheral nervous system involvement.
6. Hematologic abnormalities. The presence of lupus anticoagulant may prolong the PTT and rarely the PT secondary to its reaction with the phospholipids used in the test.[44] On the other hand, anticardiolipin antibodies detected in parturients with systemic lupus erythematosus may be associated with thrombocytopenia in addition to abnormal PTT or PT. However, patients are generally *hypercoagulable*.
7. The increased incidence of thrombosis in parturients with systemic lupus erythematosus may require anticoagulant therapy.
8. Rarely, lupoid hepatitis.

Anesthetic Management

Anesthetic management either for labor and delivery or for cesarean section will depend on the severity of the disease and

organs involved. If clotting parameters are normal, one can use regional anesthesia, but invasive monitoring may be necessary in women with severe respiratory and cardiovascular problems. General anesthesia may be necessary in the presence of clotting abnormalities. Recently, Harnett et al. have used TEG to determine the coagulation status in patients with phospholipid antibodies receiving prophylactic heparin. If the TEG's R parameter is within normal range, it suggests no significant levels of heparin in patients with laboratory evidence of prolonged PTT.[45]

Maternal Addiction

The following are among the major problems when faced with maternal opioid addiction:

1. Withdrawal symptoms occur if parturients do not receive the opioids.
2. There is an increased likelihood of perinatal mortality from maternal opioids addiction because of prematurity and low birth weight.
3. Maternal withdrawal may trigger fetal withdrawal and lead to fetal hyperactivity, an increase in oxygen consumption, and fetal hypoxia.
4. An acute drug overdosage may cause hypotension and fetal death.
5. The chance of maternal hypotension during anesthesia is greater because of adrenal insufficiency, associated hypovolemia, or the possibility of maternal overdose from opioids.
6. Starting an intravenous infusion can be difficult.

Cesarean delivery in the presence of cardiovascular, respiratory, or neurological problems secondary to addiction may occasionally make regional anesthesia unsafe. General anesthesia can be given in such situations. The majority of these patients may have associated liver problems that can prolong the duration of anesthetic medications. Inhalational agents such as sevoflurane or desflurane may be ideal due to their rapid recovery.

Active resuscitation of the neonate may also be necessary. Postoperative pain relief is always a problem in these

patients because of tolerance. The use of epidural anesthesia for postoperative pain relief might be beneficial in such cases.

Alcohol

Major Problems

Medical complications including hemorrhage because of esophageal varices and clotting abnormalities due to abnormal liver function, cardiomyopathy, neuropathy, and the possibility of increased gastric volume and gastric acidity are some of the problems to be considered before the administration of anesthesia. There is also the possibility of fetal alcohol syndrome.

Anesthetic Management

Both for labor and delivery and for cesarean delivery, epidural anesthesia is safe as long as there are no clotting abnormalities. Spinal anesthesia is also good option if there is no significant cardiac involvement. Regional anesthesia will help to minimize the chances of aspiration.

Amphetamines

Anesthetic Management

Since amphetamines are CNS stimulants, they cause depletion of CNS catecholamines and might cause a poor response to indirectly acting sympathomimetic agents like ephedrine. An increased anesthetic requirement is a possibility if one uses general anesthesia. Epidural anesthesia might be a better choice in this situation, and hypotension may be treated with small doses of phenylephrine, if ephedrine is ineffective.

Cocaine

Cocaine blocks the presynaptic uptake of norepinephrine, serotonin, and dopamine. In the CNS, it increases monoamine

neurotransmitter levels and lowers the seizure threshold.[46] "Crack" is commonly smoked at the present time, and free base cocaine is rapidly absorbed across the pulmonary blood vessels and reaches the CNS in high concentration. Severe hypertension and tachycardia can be a problem for the anesthesiologist. Because of its vasoconstriction property, cocaine will reduce uteroplacental blood flow, and abruptio placentae and labor can occur immediately following self-administration of cocaine.[47] Multiple congenital abnormalities, growth retardation, and decreased weight have been described in neonates of cocaine-addicted mothers. Placental abruption is associated with coagulation abnormalities and this should be checked before regional anesthesia.

Anesthetic Management

Labor and Delivery. Epidural analgesia is the most effective method of pain relief in cocaine-addicted parturients. Chronic cocaine use can cause thrombocytopenia and therefore platelets should be checked before placement of regional anesthesia.

Cesarean Section. Regional anesthesia should be the anesthetic of choice. Epidural anesthesia is associated with a decreased incidence of hypotension, and it can be used for effective control of postoperative pain. Hypotension has been treated with ephedrine successfully. Phenylephrine (50–100 μg) may be necessary in certain circumstances. Cocaine may decrease the plasma cholinesterase concentration and may prolong the action of 2-chloroprocaine.

General anesthesia may be necessary in the presence of acute fetal distress associated with abruptio placentae. Reflex hypertension and tachycardia during intubation can be treated with labetalol. A decreased pseudocholinesterase activity can prolong the duration of action of succinylcholine. Severe tachyarrhythmias may be associated with general anesthesia.

Infectious Diseases

Genital Herpes

Caused by herpes simplex virus (HSV) types 1 and 2, the majority of genital herpes lesions are caused by the HSV-2 virus. Most obstetric management issues revolve around possible transmission of the virus to the neonate at the time of birth. Current recommendations for obstetric management include the following (ACOG Practice Bulletin. Obstet Gynecol 2007;1029:1489):

1. The route of delivery should be determined by assessment of the lesion at the time of delivery.
2. Viral cultures are no longer recommended.
3. If no evidence of a lesion exists, vaginal delivery is recommended. The viral culture result is delivered to the pediatrician.
4. Any suggestion of a positive lesion is generally an indication for cesarean section.

Anesthetic management of a primary lesion is controversial. In the author's institution, regional anesthesia is not used if there is any indication of a primary lesion because primary HSV infections are associated with viremia and the possibility of encephalitis. In the case of secondary infection, we prefer regional anesthesia both for labor and delivery and for cesarean section even during the active phase unless contraindicated for other reasons. Bader et al. reported a 6-year retrospective survey of 169 parturients who underwent cesarean section with a diagnosis of HSV.[48] A total of 164 parturients had secondary infection, whereas 5 had a diagnosis of primary infection. Fifty-nine women had general anesthesia, 75 received spinal anesthesia, and 35 received epidural anesthesia. None of the parturients with secondary infection who received regional anesthesia had any evidence of septic or neurological complications (Fig. 14-8, Table 14-8). Convincing data exit regarding the use of intraspinal morphine and increased risk of *recurrent HSV-1 (generally oral)*. Anesthesiologists should be cautious about using the intraspinal morphine for postoperative analgesia in parturients with a history of an HSV-1 infection.

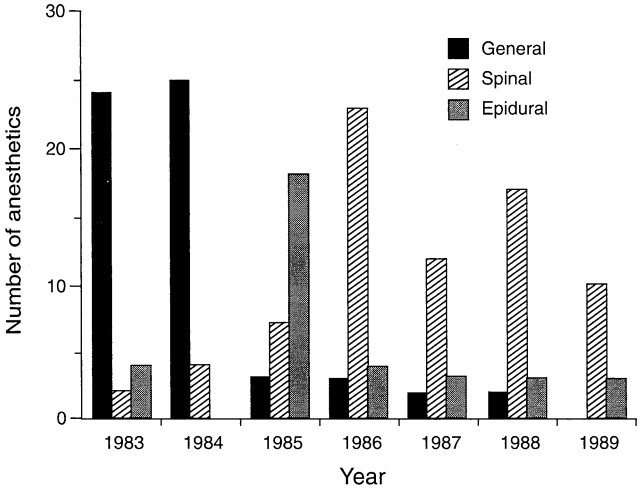

Figure 14–8. Different anesthetic techniques used for cesarean section with a diagnosis of HSV infection between 1983 and 1989. (From Bader et al.[48] Used with permission from Elsevier.)

Infection with the Human Immunodeficiency Virus

Acquired immunodeficiency syndrome (AIDS) is the end-stage condition of a disease caused by the human immunodeficiency virus (HIV). Women of reproductive age are the fastest growing population with HIV. Seroprevalence of HIV during pregnancy has been estimated to be 1.7 per 1,000 pregnancies. Common signs and symptoms have become more moderate or subclinical, and new clinical presentations have emerged. It is quite apparent that HIV disease affects multiple organ systems. Advances have been made in elucidating the pathogenesis of HIV. In addition, the molecular technique of viral load determination and the CD4+ T-lymphocyte count enable evaluation of the disease, its prognosis, and its response to therapy.

There is limited specific information concerning the overall risk of anesthesia and surgery of HIV/AIDS patients. However, as far as can be determined, surgical interventions do not

Table 14–8. Indications for Cesarean Delivery (No. of Cases by Year)

Indication	1983	1984	1985	1986	1987	1988	1989†
Active lesion present at delivery	24	27	27	26	15	20	9
Healing lesion present at delivery	1	1	–	3	–	–	3
No active lesion but positive cultures within 2 wk of delivery	3	1	1	–	1	–	1
Other	2	–	–	1	1	2	–
Total cases	30	29	28	30	17	22	13

Reprinted from Bader et al.,[48] with permission from American Society of Regional Anesthesia and Pain Medicine.

increase the postoperative risk for complications or death and therefore should not be withheld. There is also little evidence to suggest that HIV or antiretroviral drugs increase the rate of pregnancy complications or that pregnancy may alter the course of HIV infection. It should be emphasized that all practicing anesthesiologists should be familiar with the disease and should use prenatal anesthesia consultations and a team approach to assure optimal treatment for HIV patients.[49]

Anesthetic Technique

The CNS manifestations can include paralysis, ataxia, encephalitis, and coma. The virus has been isolated from the CSF from parturients with HIV.[50] Anesthesiologists should carefully look for any evidence of neurological deficit before the administration of anesthesia, and pregnant women should be told about the possibility of continuation of the neurological problems that might not be related to the anesthetic technique in any way. Regional anesthesia should not be contraindicated in a parturient with AIDS. Yet, one must take into consideration the presence of neuropathies, local infection, or blood-clotting abnormalities. General anesthesia is considered safe, but drug interactions and their impact on various organ systems should be considered preoperatively. There is a possibility of difficult endotracheal intubation due to pharyngeal lymphatic hypertrophy.[51]

Risk to the Anesthesiologist

Of all cases, 0.5% are estimated to be infected with HIV.[52] Hence, care should be taken when contact with bodily fluids is anticipated. Double gloves, mask, gown, eye wear, etc. should be used. Caution is also needed while handling needles and sharp objects.

Psychiatric Disorders

Psychiatric disorders of women of childbearing age are as follows:

I. Schizophrenia
   A. Paranoid
   B. Schizoaffective
   C. Medications commonly used:
      1. Phenothiazenes
      2. Butyrophenones
II. Bipolar disorder
   A. Manic with or without psychotic features
   B. Mixed with or without psychotic features
   C. Depressed with or without psychotic features
   D. Medications commonly used:
      1. Lithium
      2. Carbamazepine
      3. Valproic acid (Depakote)
III. Major depression with or without suicidal tendency
   A. Medications commonly used:
      1. Tricyclic antidepressants, seratonergic as well as nonadrenergic types
      2. Monoamine oxidase inhibitors
IV. Dysthymia
   A. Medications commonly used: tricyclic antidepressants
V. Miscellaneous diagnostic categories
   A. Panic disorder with or without agoraphobia
   B. Generalized anxiety disorder
   C. Anorexia and/or bulimia
   D. Post-traumatic stress disorder
   E. Obsessive-compulsive disorder
   F. Medications commonly used:
      1. Tricyclic antidepressants
      2. Benzodiazepines
      3. Phenothiazenes
      4. Monoamine oxidase inhibitors

Clinical Implications

Because of recent evidence of the relationship between neurohormonal imbalance and psychiatric disorders, various medications have been used for the treatment of different psychological problems. Drug interactions between psychotropic

medications and anesthetic techniques and agents have been discussed in Chapter 4.

Malignant Hyperthermia

Only a few cases of malignant hyperthermia during pregnancy have been reported. The clinical features of malignant hyperthermia under anesthesia include (1) hypercarbia, (2) tachycardia, (3) hypertension, (4) muscle rigidity, (5) tachypnea, (6) lactic acidosis, and (7) rapidly increasing body temperature. Recommended laboratory analyses during malignant hyperthermia are shown in Table 14-9. The hotline telephone number for the management of malignant hyperthermia is 800-644-9737. The website is www.mhaus.org.

Anesthetic Management

Regional Anesthesia

It would appear that regional anesthesia is preferable for labor and delivery as well as cesarean delivery. Currently, most anesthesiologists agree with the use of either amide

Table 14–9. Recommended Laboratory Analyses for Malignant Hyperthermia

Central Venous Blood Gas Analysis
Arterial blood gas analysis
Central venous electrolytes (Na^+, K^+ Cl^-, HCO_3^-)
Serum glucose
Central Venous Creatine Phosphokinase
and isoenzymes – immediately and every 12 h
Hemoglobin or Hematocrit Fibrinogen
and fibrin degradation products
Plasma myoglobin
Urine Myoglobin
Urine pH

From Longmire et al.[64] Used with permission from Elsevier. Essential studies shown in boldface type.

or ester local anesthetics. The addition of epinephrine to the local anesthetic is felt to be contraindicated because α-adrenergic agonists precipitate malignant hyperthermia in pigs, but this is controversial.[53] The authors have used ephedrine for the treatment of hypotension without problems, but one might consider using phenylephrine in such cases. We have also used epinephrine-containing local anesthetics for epidural anesthesia.

General Anesthesia

If general anesthesia has to be used, then one must avoid depolarizing muscle relaxants and inhalational anesthetics or other triggering agents. Dantrolene should be always readily available.

Role of Dantrolene. Dantrolene crosses the placenta, and a fetal blood level of about 60% of that of the mother is reached. There are no reports of adverse neonatal effects but it may cause transient hypotonia. Prophylaxis with dantrolene is a matter of debate. While it seems safe to administer, its use may not be necessary. If used, the prophylactic dose is 2.4 mg/kg intravenously given over a period of about 15 min preoperatively. Most authorities do not recommend prophylactic dantrolene and will avoid the agents that trigger malignant hyperthermia. Another potential problem that has been described recently in the literature is the occurrence of uterine atony following dantrolene treatment.

Obesity

The major problems associated with maternal obesity are as follows:

1. Associated medical problems like hypertension, respiratory insufficiency, diabetes mellitus, etc., are common.
2. The volume of gastric contents may be high and with a low pH. However, a recent study contradicted these findings.[54] Harter et al. found a lower incidence of combined high-volume, low-pH gastric contents in obese patients as compared to lean patients.

3. There can be technical difficulty with regional anesthesia.
4. Obstetric complications are high in this group of parturients.
5. Laryngoscopy may be difficult in such cases.
6. There is high incidence of failed epidural catheters and multiple attempts for epidural placement.

Anesthetic and obstetric outcome of 117 morbidly obese parturients were studied retrospectively. The findings included (1) higher oxytocin use, (2) higher rate of cesarean section (62% compared with 24% in the control group), (3) significantly more initial epidural anesthesia failure (42% compared with 6% in normal parturients), (4) significantly higher incidence of accidental dural puncture, and (5) increased incidence of difficult intubation.[55] Recently, a maternal mortality study (1985–2005) from Michigan showed that six out of eight pregnant women who died were obese.[56,57]

Anesthetic Management

Labor and Delivery

Epidural analgesia is preferable and should be used if technically possible. Continuous spinal analgesia has also been used with success. We prefer sitting position for epidural placement.

Elective Cesarean Section

If one considers regional anesthesia, single-shot spinal anesthesia should be used cautiously, if at all, because of the following:

1. Control of the spinal anesthetic level is unpredictable.
2. There is a very high incidence of hypotension.
3. Spinal anesthetic can reach higher levels and cause further compromise of the already abnormal pulmonary function. However, continuous spinal anesthesia may reduce these problems. For epidural anesthesia, the volume of the local anesthetic might have to be reduced. CSE technique using a small amount of local anesthetic for spinal portion may be a good option (sequential CSE). This allows flexibility of anesthetic duration.

General Anesthesia

If general anesthesia is necessary, one should carefully check the airway before the induction of anesthesia. Laryngoscopy may prove difficult in these cases because both the chest and large breasts often impede the use of the usual laryngoscope handle. Use of a short-handle laryngoscope (Datta-Briwa) can circumvent this problem (Fig. 14-9). Awake intubation using a laryngeal mask airway has been described. Special laryngoscopes like Bullard's laryngoscopes such as Bullard have been used in morbidly obese pregnant women.[58]

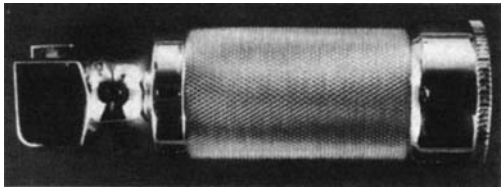

Figure 14–9. Datta-Briwa short-handle laryngoscope.

Summary

With increasing number of parturients with comorbid diseases reaching childbearing age, a thorough understanding of pathophysiology of the disease process is essential to determine the ultimate effect of physiological changes of pregnancy on the parturient. Occasionally, the physiological changes of pregnancy can tilt the delicate balance of well-being towards the side of clinical decompensation. When this occurs, a multimodal team approach is the key to safely maneuver the parturient through the pregnancy, delivery, and postpartum period.

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15
High-Risk Pregnancy: Pregnancy-Related Problems

S. Datta et al., *Obstetric Anesthesia Handbook*,
DOI 10.1007/978-0-387-88602-2_15,

A parturient is designated as "high risk" because of the various problems that might arise in the antenatal or peripartum periods. Anesthetic management should be based on a thorough understanding of the physiology of pregnancy and also on the pathophysiology of the problems that made the parturients "high risk." Any high-risk parturient can suffer an obstetric emergency. Hence, continuous vigilance and constant communication with the obstetric team is mandatory.

Maternal-Related Issues

Antepartum Hemorrhage

Antepartum hemorrhage is a major cause of maternal mortality in the obstetric patient. Severe bleeding during the antepartum period is usually due to placenta previa or abruptio placentae.

Placenta Previa

Placenta previa is classified into three groups[1] (Fig. 15-1):

1. *Complete Previa* (37%) – the internal os is completely covered.
2. *Partial Previa* (27%) – the internal os is partially covered.

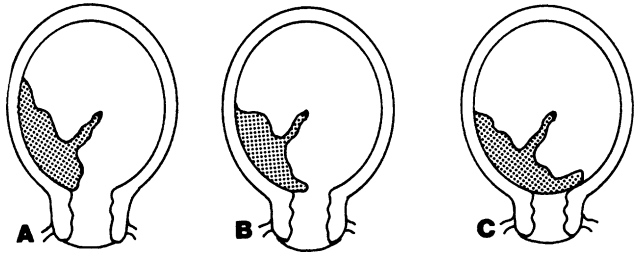

Figure 15-1. Classification of placenta previa. **(a)** Low-lying placenta. **(b)** Incomplete placenta previa. **(c)** Complete placenta previa. (From Bonica and Johnson[78] with permission)

3. *Marginal Previa* (*37%*) – part of the internal os is encroached on by the placenta.

The incidence varies between 0.1 and 1%. Bleeding is caused by tearing of the placenta and its detachment from the decidua.

Anesthetic Management of Actively Bleeding Parturient. If the parturient is actively bleeding, emergency cesarean delivery should be performed, usually under general anesthesia. Blood, plasma, and crystalloids should be infused as rapidly as possible as determined by the blood pressure, pulse rate, hematocrit, urine output, and coagulation abnormalities. Induction of anesthesia may include a small dose of etomidate and/or ketamine if there is significant hypotension.

Because of the rising incidence of repeat cesarean sections, the incidence of placenta accreta, increta, and percreta has increased in recent years. *Placenta accreta* includes adherence of placenta to the uterine wall, *placenta increta* involves the invasion of placenta into the myometrium, and *placenta percreta* includes the placenta invading through the myometrium. A significant number of these women might end up having cesarean or postpartum hysterectomies. Parturients with previous caesarean sections and placenta previa should be treated carefully: one or more large-bore intravenous lines, a warming blanket, and blood for an immediate transfusion should be ready. Clark and colleagues observed the relationship between the number of previous caesarean sections and the subsequent

occurrence of placenta accreta.[2] The incidence of placenta accreta from placenta previa with one prior cesarean section was 24%, whereas it was as high as 67% with four or more previous cesarean sections. The incidence of accreta is about 5% when an unscarred uterus is associated with placenta previa. The ideal anesthetic technique for this procedure is controversial, but the following outline lists the advantages and disadvantages of regional versus general anesthesia:

I. Regional anesthesia
   A. Advantages
      1. Less blood loss.[3]
      2. Awake patient with less chance of aspiration; parturient will be able to experience delivery of baby.
   B. Disadvantages
      1. Peripheral vasodilation may exacerbate hypotension.
      2. General anesthesia may be necessary for patient's comfort if a cesarean hysterectomy is necessary. *Chestnut and colleagues*[4] *reported on 12 parturients out of 46 who underwent cesarean hysterectomy under epidural anesthesia, none of whom needed general anesthesia.* The rest of the patients (34) received general anesthesia from the start of the operation.

II. General anesthesia
   A. Advantages
      1. Hemodynamic stability.
      2. Security of the airway from the onset of surgery.
      3. Avoids the discomfort to the patient as a result of extensive abdominal surgery with Trendelenburg position under regional anesthesia.
   B. Disadvantages
      1. Chance of a difficult intubation, inability to intubate, and possible gastric aspiration.
      2. Unconscious patient not able to participate in the birthing process.

Anesthetic Management of a Parturient not Actively Bleeding. Regional anesthesia (subarachnoid or epidural block) may be used if the parturient so desires, provided that

there is no evidence of hypovolemia. Epidural or combined spinal epidural anesthesia is preferable in repeat cesarean section with previa or when placenta accreta is suspected, because it will provide flexibility for the extended duration of the surgical procedure. To minimize bank blood transfusions, the following options have been used: (1) Acute hemodilution – in this technique about 750–1,000 ml of blood is obtained from the parturient before the cesarean section and replaced by equal volume of 6% hetastarch under continuous fetal heart rate and maternal hemodynamic monitoring. The collected blood is then transfused either during or on completion of the surgery.[5] (2) Various studies have observed that the cell saver technique can filter away tissue factor, lamellar bodies, fetal squamous cells and alpha fetoprotein. A few studies have shown success of this method with no increased incidence of adult respiratory distress syndrome, amniotic fluid embolism, disseminated intravascular coagulation, infection or length of hospital stay.[6,7] This may be a method of choice in pregnant women who refuse homologous blood transfusion. (3) Selective arterial embolization is becoming popular to control obstetric hemorrhage. Although not subjected to randomized trials, it appears to have a high success rate in avoiding massive hemorrhage and hysterectomy. The procedure is done by an interventional radiologist under fluoroscopic guidance. Depending upon the indications, it can be done using regional, general anesthesia, or conscious sedation.[8] We have recently improvised this technique further by performing the cesarean delivery in the Interventional Radiology suites. Arterial balloon catheters are placed into the uterine arteries under epidural anesthesia. After cesarean delivery, the balloons are inflated if bleeding occurs as a result of placenta accreta. The interventional radiologist embolizes the uterine arteries if necessary. If the procedure successfully controls the bleeding, it gives an opportunity to avoid hysterectomy and offers the possibility of future pregnancies.[9]

Abruptio Placentae

Abruptio placentae is a premature separation of a normally implanted placenta from the decidua basalis (incidence,

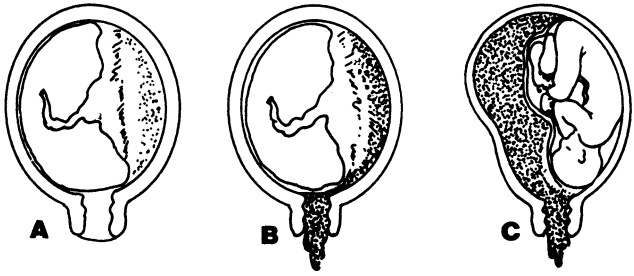

Figure 15-2. Classification of abruptio placentae. (**a**) Concealed hemorrhage. (**b**) External hemorrhage. (**c**) External hemorrhage with prolapse of the placenta. (Bonica and Johnson[78] with permission)

0.2–2%)[1] (Fig. 15-2). It is classified as mild, moderate, or severe. Bleeding might be concealed, with the blood retained behind the placenta, or revealed, with the blood flowing externally. *Severe abdominal pain with fetal distress may be the initial clinical findings.* Use of cocaine or crack may be associated with abruptio placentae.

Anesthetic Management. If there is active bleeding, the management is similar to as in placenta previa. Abruptio placentae may be associated with blood coagulation defects and is a common cause of coagulopathy in pregnancy. Diagnostic tests include hemoglobin/hematocrit, platelet count, fibrinogen level, prothrombin time (PT), and partial thromboplastin time (PTT). *If there is no evidence of maternal hypovolemia or uteroplacental insufficiency and if the clotting studies are normal, continuous epidural anesthesia may be used for labor and vaginal delivery.* In severe abruption, emergency delivery may need to be performed under general anesthesia. A massive and rapid blood transfusion might be necessary. If the infant is alive at delivery, active resuscitation is usually required because of the maternal and fetal hypovolemia resulting in neonatal hypovolemic shock.

Table 15-1 compares the clinical presentation of placenta previa and abruptio placentae. Besides the clinical features, confirmation of the diagnosis is made by ultrasound; however,

Table 15-1. Differential Diagnosis (Placenta Previa vs. Abruptio Placentae)

Clinical Features	Placenta Previa	Abruptio Placentae
Bleeding	Painless	Painful
Blood	Fresh	Dark, old, mixed with clots
Clotting problems	Uncommon	Common
Sudden fetal distress	Uncommon	Common

occasionally a double setup, in which vaginal examination is performed in the operating room with preparation for immediate cesarean section, may be necessary to confirm low-lying placenta previa. Anesthetic management for a double setup should include the following:

1. The parturient should be prepared for proceeding with general anesthesia
2. Cross matching of at least 2 units of blood
3. Two large-bore intravenous lines
4. Provision for arterial line placement
5. Preoxygenation

If a placenta previa is detected, cesarean section may be accomplished under regional anesthesia; if, however, bleeding ensues following vaginal examination, immediate general anesthesia is used for prompt delivery.

Postpartum Hemorrhage

Uterine atony is the most common cause of postpartum hemorrhage, and drugs used in its management are discussed in Chapter 4. It complicates 10% of pregnancies and accounts for approximately 70% of postpartum hemorrhage. The predisposing factors include rapid and protracted delivery, tocolysis, overdistension of uterus (macrosomia, multiple gestation, polyhydramnios), prolonged oxytocin infusion, retained placenta, operative vaginal delivery, chorioamnionitis, and general anesthesia. Bimanual examination (one hand in the vagina and the other over the abdomen) usually confirms the diagnosis and uterine massage is enough to promote uterine involution in

majority of cases. Uterine contraction and involution can be promoted with uterotonic agents such as oxytocin, methylergonovine, 15-methyl prostaglandin F2-alpha, or misoprostol. The details of these drugs have been discussed in Chapter 4.

Four other main causes of postpartum hemorrhage are laceration, retained placenta, uterine inversion, and uterine rupture.

Lacerations

Lacerations of the cervix, vagina, and perineum are the second most common cause of postpartum hemorrhage. Blood loss is often underestimated in these women and resuscitation of blood volume is a vital component of management. Anesthesia may be provided by an indwelling epidural catheter if present and if the patient is hemodynamically stable. Spinal or local anesthesia are alternatives in stable patients without epidural catheters. General anesthesia should be used in unstable patients.

Retained Placenta

Retention of the placenta or placental fragment is the third most frequent cause of postpartum hemorrhage. *Anesthetic management* will depend upon the severity of bleeding and cardiovascular stability. Obstetric management may include manual extraction of the placenta or ultrasound guided vacuum or sharp curretage. In the presence of severe bleeding the following steps are necessary:

1. Two large-bore intravenous lines.
2. Two units of ABO Rh type-specific cross-matched blood should be immediately requested, and the blood bank should be alerted about the possibility of hemorrhage.
3. Intravenous Ringer's lactate and 5% albumin or 6% hetastarch should be used rapidly.
4. Vasopressors may be necessary.
5. Uterine relaxation may be required. Traditionally, this was accomplished with inhalation anesthetics. More recently intravenous nitroglycerin up to 500 μg has been used for uterine relaxation with great success.[10] We prefer

to use 50–100 μg of nitroglycerin in the first instance after adequate volume replacement. Vigilant blood pressure monitoring is mandatory when using nitroglycerin.

Epidural Anesthesia. If possible, establishment of adequate epidural anesthesia via an indwelling epidural catheter is the technique of choice at Brigham and Women's Hospital.

Subarachnoid Block. If the parturient does not already have epidural anesthesia instituted, then subarachnoid anesthesia may be used, assuming normal hemodynamic status of the parturient.

Intravenous Sedation. In some cases a small amount of midazolam (1–2 mg) and fentanyl (50–100 μg) will help to facilitate placental extraction by providing pain relief. If this technique does not provide suitable conditions for placental extraction, regional anesthesia or general anesthesia should be contemplated.

General Anesthesia. If the cardiovascular situation contraindicates the use of regional anesthesia, then general endotracheal anesthesia should be used. Induction agents should include, depending on the hemodynamic condition, thiopental, propofol, etomidate, or ketamine.

Inhalation anesthetic may be necessary to relax the uterus. However, the inhalation anesthetic should be decreased or discontinued as soon as possible to prevent uterine relaxation and hemorrhage. At this time, adequate depth of anesthesia should be ensured using alternative techniques. Bispectral Index (BIS) monitoring may be helpful under these circumstances.

Uterine Inversion

Uterine inversion is a rare complication that can be associated with massive hemorrhage (Fig. 15-3). Hemorrhage and shock are common findings. For acute inversion, ongoing epidural or spinal anesthesia can be used provided that the patient is hemodynamically stable; however, in the presence of subacute or chronic inversion, uterine relaxation with an inhalation anesthetic may be necessary, and general anesthesia will become essential. Nitroglycerin may also be used to relax the uterus; however, the blood pressure should be closely

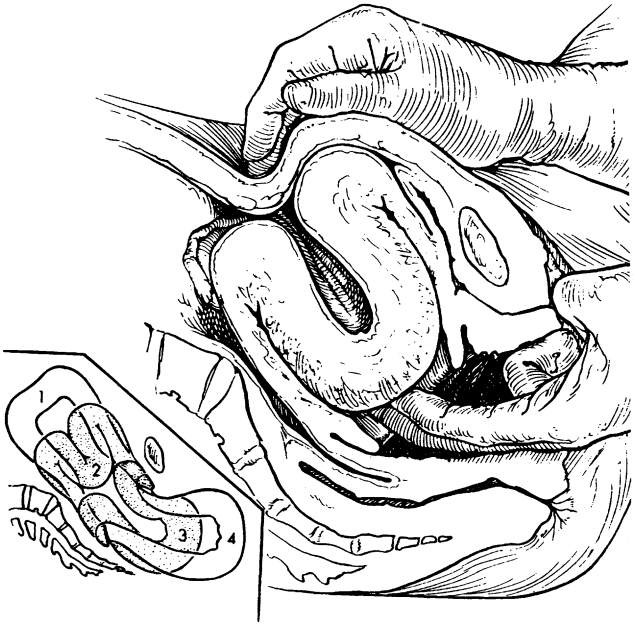

Figure 15-3. Incomplete inversion of the uterus. (From Cunningham et al.[79])

monitored. Shah-Hosseini and Evrad have published the incidence of uterine inversion that occurred between 1978 and 1988 in the Women and Infants' Hospital of Providence, Rhode Island.[11] Out of 70,481 deliveries, 11 women had uterine inversion (1 in 6,407), and 73% of the parturients were nulliparous. The overall estimated blood loss varied from 150 to 4,300 mL. Anesthetic techniques included (1) local anesthesia, (2) epidural anesthesia, and (3) general anesthesia using thiopental, ketamine, and in a few cases, halothane was used (for uterine relaxation). In one case, surgery was necessary to reduce the inversion. The authors concluded that early diagnosis, adequate volume therapy, and immediate correction of inversion are absolute essential factors for a good outcome.

Uterine Rupture

Uterine rupture most commonly occurs from a previous uterine scar from either cesarean section or uterine surgery. Trophoblastic invasion of the uterus can also be an important factor in uterine rupture. Cesarean hysterectomy may be indicated in a few occasions. Thus parturients undergoing vaginal delivery after previous cesarean section or following uterine surgery should be closely monitored. A suspicion of uterine rupture should be also in the differential diagnosis in the event of a fetal bradycardia in patients at risk.

Vaginal Birth After Cesarean Delivery (VBAC) (also called Trial of Labor After Cesarean Delivery; TOLAC)

American College of Obstetricians and Gynecologists (ACOG) bulletin 54 recommends VBAC or TOLAC to decrease unnecessary cesarean deliveries.[12] One of the important recommendations is that the hospital undertaking VBAC deliveries should have the capacity to perform emergency cesarean section within 30 min.

Anesthetic Management

A uterine scar is susceptible to uterine rupture during labor and delivery. Epidural analgesia for labor and delivery was relatively contraindicated in the past for two main reasons: (1) masking of pain from uterine rupture because of epidural blockade and (2) blunting of sympathetic responses because of ongoing epidural analgesia.[13] However, a few studies using 0.25–0.37% bupivacaine showed that these concentrations of local anesthetic did not relieve the continuous pain of a ruptured uterus.[14–16] Crawford concluded that pain from a ruptured uterus should "break through" a previously established epidural anesthetic. In addition, further studies showed that abdominal pain and tenderness may not be specific and sensitive signs of uterine scar separation: Golan and colleagues observed that uterine or uterine scar tenderness was an infrequent presentation of uterine rupture.[17] Fetal distress as well

as cessation of uterine activity are more reliable signs for separation of a uterine scar. Therefore, presently the majority of anesthesiologists as well as ACOG do not consider epidural analgesia to be contraindicated for vaginal birth after cesarean section. Furthermore, Demianczuk and colleagues suggested a few advantages of epidural analgesia during this procedure:[18] (1) it enables palpation of the scar during labor; and (2) it permits bimanual examination of the uterus to examine the scar after delivery. In summary, epidural analgesia may be used for vaginal birth after cesarean section; however, continuous fetal heart rate monitoring and continuous measurement of the intensity of uterine contractions should be used, and a low concentration of local anesthetic for epidural analgesia may also be beneficial.

Pregnancy-Induced Hypertension

Definition and Terminology

Hypertension during pregnancy is a common medical problem that occurs in approximately 250,000 American women every year. This disease is associated with an increased incidence of maternal, fetal, and neonatal mortality and morbidity, compared to normal parturients. The ACOG classifies hypertension during pregnancy into four subgroups:

1. Preeclampsia, eclampsia
2. Chronic hypertension
3. Chronic hypertension with superimposed preeclampsia (or eclampsia)
4. Gestational hypertension

ACOG has updated the definition of hypertension related to preeclampsia. Hypertension is defined as a sustained blood pressure increase to levels of 140 mm Hg systolic or 90 mm Hg diastolic. Blood pressure should be measured in sitting position. In preeclampsia, a parturient should have two clinical findings; (1) hypertension (2) proteinuria. These should occur after the 20th week of gestation. Preeclampsia complicates about 6–8% of pregnancies. If the preeclampsia is associated with convulsions, then the term is changed to eclampsia. Preeclampsia *more frequently occurs in very young or elderly*

primigravidas. Parturients will be included in the category of severe preeclampsia if they have any of the following clinical findings: (1) systolic blood pressure of 160 mm Hg or higher, (2) diastolic blood pressure of 110 mm Hg or higher, (3) proteinuria of 5 g/24 h or more, (4) oliguria with 500 mL or less of urine output in 24 h, (5) cerebral and visual disturbances, seizures, (6) epigastric pain, (7) pulmonary edema or cyanosis, or (8) HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count). The main causes of maternal mortality are (1) cerebral hemorrhage (30–40%), (2) pulmonary edema (30–38%), (3) renal failure (10%), (4) cerebral edema (19%), (5) disseminated intravascular coagulation (9%), and (6) airway obstruction (6%).

Pathogenesis

Maternal endothelial cell dysfunction has been thought to be the primary underlying process resulting in preeclampsia.[19] There is an increased concentration of the markers for endothelial cell activation in preeclampsia. In normal pregnancy, the trophoblast cells invade into the decidualized endometrium and the inner third of the myometrium. This process occurs within the first 18 weeks of pregnancy. During this time, the endothelium, the internal elastic lumina, and the muscular layer of the medial of the spiral arteries, which supply the placenta, are replaced by trophoblast cells. These changes result in a vascular supply characterized by decreased vascular resistance and high flow. This allows increased blood flow to the intervillus space and adequate gas and nutrient exchange to the fetus. In preeclampsia, however, the trophoblastic invasion into the spiral arteries is incomplete and may not undergo endovascular trophoblast invasion, resulting in intact myometrial segments. In addition, there is acute atherosis leading to thrombosis of the vessels. A combination of these two factors result in the hallmark feature of preeclampsia, placental insufficiency.

Oxidative stress that is brought about through a number of pathways in preeclamptic women has been incriminated as one of the causes of endothelial dysfunction.[20] There are increased levels of low density lipoprotein (LDL) in subendothelial spaces

where they bind to proteins and phospholipids and signal the recruitment of monocytes. This leads to lipid peroxidation which in turn leads to membrane damage. Free radicals and lipid peroxidases can inhibit prostacyclin production, increase thomboxane synthesis, inhibit nitric oxide production, and alter capillary permeability. The widespread membrane damage leads to edema and proteinuria found in preeclamptic pregnant women.

Genetic influences have also been reported in preeclampsia. Polymorphisms in the genes controlling the expression of inflammatory mediators such as interleukins have been described.

There are several risk factors for the development of preeclampsia. They include chronic renal disease, chronic hypertension, family history of preeclampsia, nulliparity, advanced maternal age >35 years, diabetes mellitus, African race, and multiple gestation.

Pathophysiology

The pathophysiology of preeclampsia is summarized in Fig. 15-4. Intravascular volume and protein content are markedly lower in severe preeclampsia than in normal pregnancy. There is associated vasoconstriction, possibly caused by increased circulating levels of renin, angiotensin, aldosterone, catecholamines, thromboxane, and endothelin (Table 15-2, Fig. 15-5). These circulating vasoactive substances make preeclamptic–eclamptic patients sensitive to vasoconstricting drugs, and thus vasopressors such as ephedrine should be used cautiously.

Kambam et al.[21] (Table 15-3) observed a difference regarding the P_{50} values of normal parturients and preeclamptic women. The authors concluded that in normal pregnant women there was a significant shift of P_{50} to the right as compared with nonpregnant women and that the extent of the shift to the right was directly related to the duration of pregnancy. However, the preeclamptic parturients showed a significant shift of P_{50} to the left when compared with normal pregnant women at term. Hypovolemia may decrease placental perfusion, and this together with the impaired placental function and

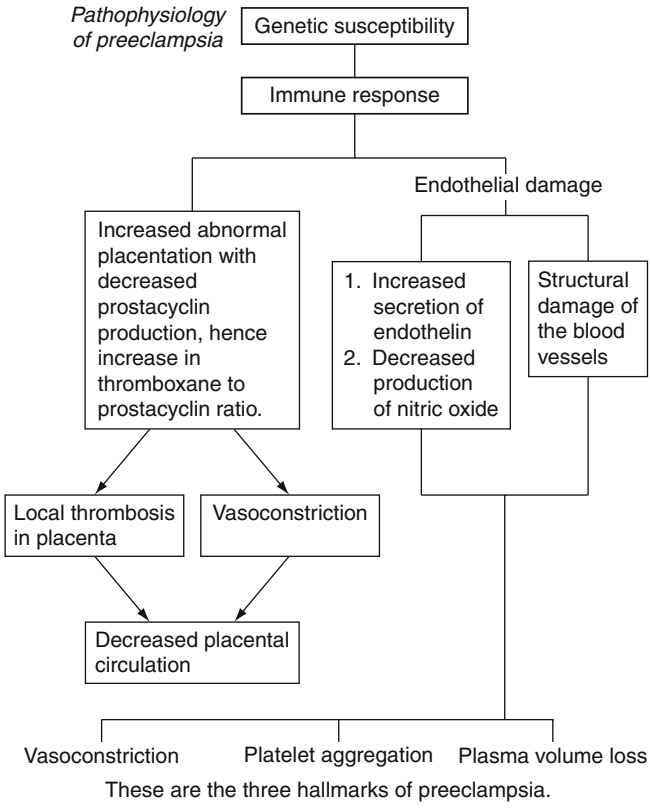

Figure 15-4. Pathophysiology of preeclampsia.

Table 15-2. Clinical Effects of Prostacyclin vs. Thromboxane

Prostacyclin	Thromboxane
Vasoconstriction↓	Vasoconstriction↑
Platelet aggregation↓	Platelet aggregation↑
Uterine activity↓	Uterine activity↑
Uteroplacental blood flow↑	Uteroplacental blood flow↓

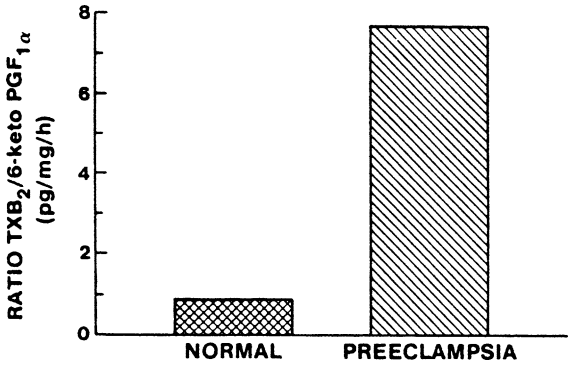

Figure 15-5. Ratio of the placental production rates of thromboxane to prostacyclin in normal and preeclamptic pregnancies. (From Walsh[80] used with permission from Elsevier.)

Table 15-3. P_{50} Values of Nonpregnant, Pregnant, and Preeclamptic Subjects

Subjects		P_{50} (mm Hg)	
Status	***n***	**Mean**	**SEM**
Nonpregnant†	10	26.7	0.11
Pregnant			
1st trimester†	10	27.8	0.08
2nd trimester†	10	28.8	0.17
At or near term†	24	30.4	0.20
Preeclamptic‡	14	25.1	0.38

†All means are significantly different from one another ($p < 0.01$), Newman-Keul's test.
‡Significant level of difference between pregnant at term and preeclamptic at term ($p < 0.001$).
From Kambam et al.[21] used with permission.

shifting of the maternal P_{50} to the left can cause a decrease in the transplacental exchange of respiratory gases.

The disease process can involve other organs as well. Liver involvement can result in coagulation abnormalities, and kidney involvement will cause oliguria and azotemia. In addition,

surface-mediated platelet activation favoring platelet adhesion to the damaged endothelial lining of vasculature results in a vicious cycle of promoting further platelet aggregation. The end result of this is a consumption coagulopathy and disruption of microvascular circulation in various organs.[22,23] Severe vasospasm of retinal vessels may be associated with visual disturbances. Magnesium sulfate or hypotensive medications may relieve this clinical feature. On the other hand, occasionally there may be associated cerebral edema and increased intracranial pressure.

The laryngeal edema of normal pregnancy can be aggravated, sometimes resulting in stridor.

Magnesium Therapy

In the United States, parenterally administered magnesium is considered the drug of choice in controlling preeclampsia and eclampsia. The normal plasma magnesium level is 1.5–2.0 mEq/L. The therapeutic range occurs at 4–8 mEq/L. Loss of deep tendon reflexes occurs at 10 mEq/L, ECC changes (prolonged PQ, widened QRS complex) appear at 5–10 mEq/L, respiratory paralysis is observed at 15 mEq/L, and ultimately cardiac arrest can occur at 25 mEq/L (Table 15-4). Magnesium sulfate therapy can potentiate both depolarizing and nondepolarizing muscle relaxant activity.[24] Magnesium is the accepted

Table 15-4. Effects of Increasing Plasma Magnesium Levels

Plasma Mg (mEq/L)	Effects
1.5–2.0	Normal plasma level
4.0–8.0	Therapeutic range
5.0–10	Electrocardiographic changes (PQ interval prolonged, QRS complex widens)
10	Loss of deep tendon reflexes
15	Sinoatrial and atrioventricular block
15	Respiratory paralysis
25	Cardiac arrest

From Shnider and Levinson[83] used with permission.

specific medication for the prevention of recurrent convulsion (eclampsia).[25,26] The beneficial effect of magnesium sulfate for this pathology is multifactoral. Both in-vivo and in-vitro studies show magnesium to increase production of the endothelial vasodilator prostacyclin. Magnesium also can protect against ischemic cellular damage by substitution for calcium and so prevents the entry of calcium ions into ischemic cells. Finally magnesium may be anticonvulsant by acting as an N-methyl-D-asparate (NMDA) receptor antagonist.[26] It also has an inhibitory effect at the neuromuscular junction.

Fluid Balance and Cardiovascular Function

A good understanding of pathophysiology of fluid balance and hemodynamic function in preeclamptic women is essential. In general, preeclampsia is a high cardiac output state associated with inappropriately high peripheral resistance. There is a decrease in overall vascular capacitance as evidenced by normal CVP and pulmonary capillary wedge pressure (PCWP) measurements.[27] Left ventricular function as illustrated by plotting the Starling curve is shifted upwards and left.[28] These findings correlate with the physical examination of patients, who usually have tachycardia, bounding pulses, wide pulse pressure, a hyperdynamic precordium, a systolic flow murmur, and warm extremities.[27] The severity of preeclampsia may dictate the relationship between CVP and PCWP. In one study, this relationship was $r=0.59$ with the overall difference between CVP and wedge pressure averaging 6 $\pm$1 mm Hg in either direction.[28] However, in a small subset of individuals with severe preeclampsia, this difference may exceed 10 mm Hg (PCWP higher) and these patients may have an increased risk of developing pulmonary edema. Under these circumstances CVP may not correlate with pulmonary capillary wedge pressure during the course of labor and epidural anesthesia.[29] Aggressive volume expansion in such women may lead to pulmonary edema. Reduction of the systemic vascular resistance (SVR) with arteriolar vasodilators should be the initial treatment in such relatively unusual cases. This subgroup of patients may also have left ventricular dysfunction contributing to pulmonary edema.[30]

Benedetti et al.[30,31] reported the etiology of pulmonary edema in 10 severely preeclamptic parturients, 20% of whom had left ventricular dysfunction as shown by an increased pulmonary artery wedge pressure associated with a low ventricular stroke work index. Thirty percent of the cases (3/10) of pulmonary edema were due to altered capillary permeability, and the diagnosis was made by observing a normal pulmonary artery wedge pressure and a normal or elevated left ventricular stroke work index (normal left ventricular stroke work index, 55–85 g/min/m^2). Finally, 50% of the cases of pulmonary edema were due to low oncotic forces with normal left ventricular stroke work. Normal colloid oncotic pressure during pregnancy is 22 mm Hg; colloid oncotic pressure can be reduced significantly in parturients with pregnancy-induced hypertension. A clinically useful estimate of the net intravascular fluid filtration pressure (i.e., the pressure tending to drive fluid out of the vessel) can be obtained by simply subtracting the pulmonary capillary wedge pressure from the plasma colloid oncotic pressure. The normal gradient in nonpregnant individuals ranges from 9 to 17 mm Hg. A decrease in the gradient to below 5 mm Hg either by an increase in the pulmonary capillary wedge pressure or a decrease in the colloid oncotic pressure can result in pulmonary edema. Thus in women in whom oncotic pressure is low, colloidal fluids may be used for intravenous volume expansion with proper monitoring.

Another major concern in these women is the increased incidence of oliguria. Clark and colleagues[32] classified the etiology of oliguria in 9 severely preeclamptic women (Fig. 15-6) into three classes. Parturients exhibiting oliguria received a fluid challenge consisting of 300–500 mL of lactated Ringer's solution or half-normal saline solution administered over a period of 20 min. In category I, the most common type, the hemodynamic profile was one of hyperdynamic left ventricular function, low to low-normal pulmonary capillary wedge pressure, and only a moderate increase in systemic vascular resistance. Oliguria in this population appeared to be on the basis of relative intravascular volume depletion in the face of systemic arteriospasm. In category II, persistent oliguria with concentrated urine in the presence of essentially normal systemic vascular resistance suggested renal hypoperfusion

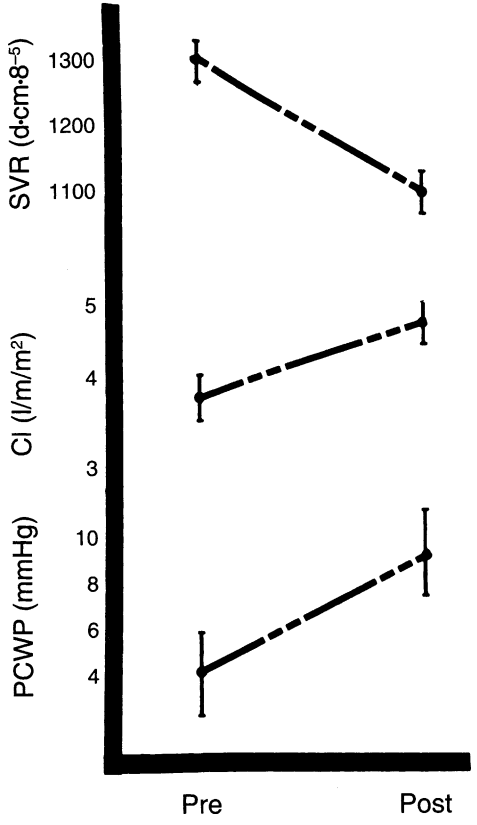

Figure 15-6. Hemodynamic changes following volume expansion in category I. *PCWP* = pulmonary capillary wedge pressure; *SVR* = systemic vascular resistance. Volume infusion resulted in decreased systemic vascular resistance, elevation of pulmonary capillary wedge pressure and cardiac index, and resolution of the oliguria, without changes in mean arterial pressure. (Adapted from Clark et al.[32])

caused by a selective degree of renal arteriospasm beyond that reflected in the measurement of systemic vascular resistance. The administration of hydralazine and, in parturients with normal pulmonary capillary wedge pressure, cautious fluid

administration resulted in resolution of the oliguric phase. In category III, a single woman exhibited a hemodynamic picture of depressed left ventricular function (low left ventricular stroke work index), elevated pulmonary capillary wedge pressure, and marked elevation of systemic vascular resistance. Oliguria appeared to be on the basis of decreased renal perfusion secondary to intense vasospasm and diminished cardiac output. In such parturients, fluid restriction with aggressive SVR reduction is indicated. SVR reduction by arteriolar vasodilators was evaluated in three pregnant women with severe preeclampsia by Strauss et al. (Fig. 15-7).[30] Pulmonary capillary wedge pressure was monitored in these patients. Vasodilator therapy produced an immediate and dramatic improvements. The initial effect

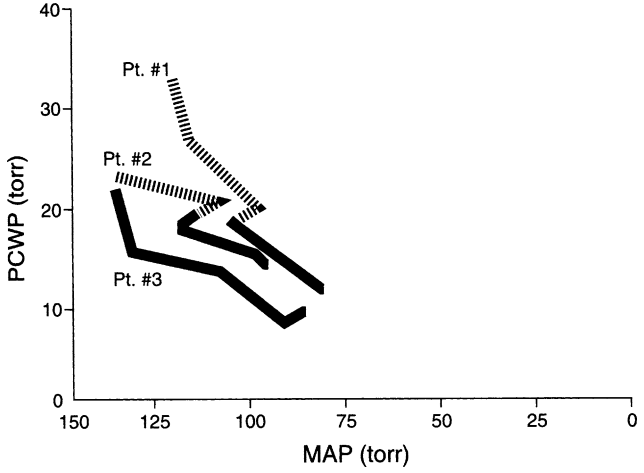

Figure 15-7. Correlation between pulmonary capillary wedge pressure (*PCWP*) and mean arterial pressure (*MAP*) during vasodilator therapy. *Interrupted line,* before cesarean section; *solid line,* after cesarean section. In a small subset of patients with preeclampsia, where the left ventricular failure is associated with high SVR, administration of arteriolar dilators produces increases in cardiac output (almost by 100%) without a significant change in blood pressure or pulse. (Adapted from Strauss et al.[30])

of relatively low-dose therapy was a near doubling of cardiac output without significant change in blood pressure or pulse.

In summary, the fluid management in a preeclamptic depends on where the hemodynamic status lies on the spectrum of hemodynamic variations described above (Fig. 15-8). The majority of the parturients with preeclampsia respond to fluid boluses as they have hyperdynamic left ventricular performance, elevated SVR, and low-normal PCWP. When these patients develop pulmonary edema, it is usually on the basis of capillary permeability or low oncotic pressure. On the other hand, a small subset of parturients may develop pulmonary edema from relative fluid overload in relation to decreased vascular capacitance and diminished left ventricular function in the presence of decreased colloid oncotic pressure. Volume loading with crystalloid and colloid prior to the induction of spinal, combined spinal epidural, or epidural anesthesia might be necessary, and when this is expertly done with adequate

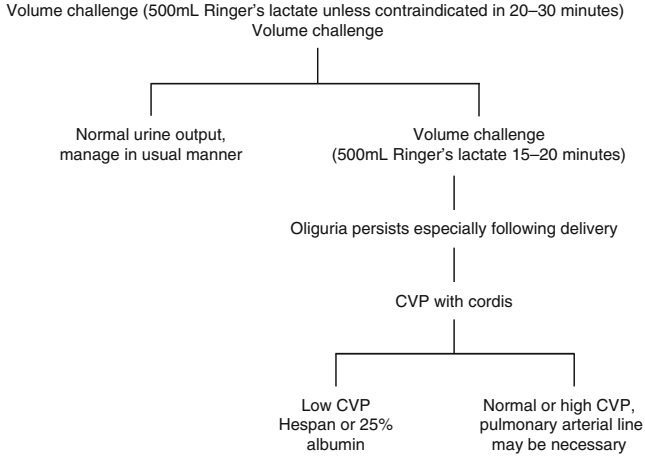

Figure 15-8. Schematic approach to fluid therapy in preeclampsia.

hemodynamic monitoring, it is safe for both the fetus and the mother.

Monitoring

A controversy that may exist regarding the treatment of preeclamptics is related to invasive monitoring. Monitoring of severely preeclamptic parturients can be subdivided into the following categories:

A. *Noninvasive*
   a. Oxygen saturation monitoring
   b. Automatic blood pressure and pulse monitoring
   c. Urinary catheter for urine output
   d. Fetal heart rate monitoring
B. *Invasive monitoring (rarely required)*
   a. Arterial line
      1. Morbidly obese woman
      2. Refractory hypertension where sodium nitroprusside or nitroglycerin is necessary because other hypotensive agents were not effective
      3. Pulmonary edema where serial blood gas measurements may be necessary
C. *Central venous pressure (CVP) monitoring*
   Severe preeclampsia with oliguria not responding to conventional fluid boluses.
D. *Pulmonary arterial (PA) – This may be required very rarely in preeclamptics as described above.*
   1. If the initial CVP reading is high (8 or above)
   2. Oliguria persists even with normal CVP and no improvement with fluid boluses
   3. Pulmonary edema in the setting of a high CVP
   4. Cardiovascular collapse

Anesthetic Management

Epidural Analgesia. For vaginal delivery epidural analgesia has the distinct advantage of relieving labor pain. Epidural

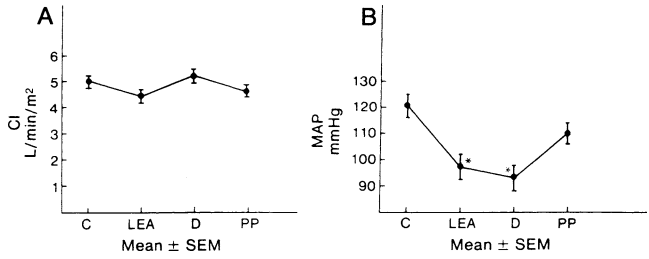

Figure 15-9. Effect on mean maternal artery blood pressure (*MAP*) following epidural anesthesia in severe preeclamptic patients. (From Newsome et al.[29] used with permission.)

analgesia will decrease maternal blood pressure (Fig. 15-9) and can indirectly increase placental perfusion[33,34] by decreasing circulating catecholamine levels. Epidural analgesia may also improve renal blood flow. However, one must make sure that the clotting parameters are normal before using epidural analgesia. Although the incidence of frank disseminated intravascular coagulation is not high in parturients with preeclampsia, coagulation abnormalities can occur in the presence of decreased platelet counts, increased fibrin split products, and slightly prolonged PTT values. Kelton et al.[35] observed thrombocytopenia in 34% of 26 preeclamptic patients. Five of these women had a prolonged bleeding time. However, the most interesting observation was that 4 parturients with normal platelet counts had prolonged bleeding times (more than 10 min). *The authors concluded that a significant proportion of women with preeclampsia develop an acquired defect of platelet function that could contribute to prolonged bleeding time. However bleeding time is not performed at the present time as it does not correlate with clinically observed bleeding.*

There is controversy regarding clotting parameters and use of regional anesthesia. If the platelet count is just less than 100,000 mm^3 with no history of abnormal bleeding (and no history of abnormal PT or aPTT), regional anesthesia can be used both for labor, delivery and cesarean section. If the platelet count is less than 75,000 mm^3 DeBoer and colleagues[36] reported laboratory evidence of coagulopathy in

10% of preeclamptic women and 30% of severely preeclamptic parturients. Clinically significant coagulopathy has been observed in 5% of mildly preeclamptic women and in 15% of severely preeclamptic parturients. Recently, thromboelastography (TEG) has been employed in evaluating coagulation status in several conditions. This is a dynamic method that studies the viscous-elastic properties of the clotting in process. The clotting process is evaluated globally rather than one individual factor. However, each component of the thromboelastogram can represent the individual contribution of various factors involved in the clotting process. Figure 15-10 shows a normal TEG,

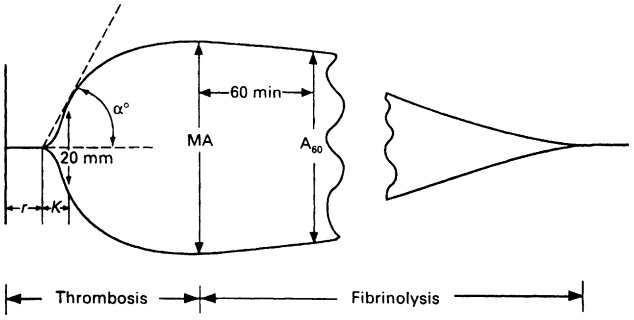

Figure 15-10. Analysis of thromboelastograph (TEG). (1) r = reaction time (normal range = 6–8 min). This represents the rate of initial fibrin formation and is related functionally to plasma clotting factor. (2) K = clot formation time (normal range = 3–6 min). The coagulation time represents the time taken for a fixed degree of viscoelasticity to be achieved by the forming clot as a result of fibrin build-up and cross-linking. It is affected by the activity of intrinsic clotting factors, fibrinogen, and platelets. (3) ($\alpha°$ [normal range = 50–60°] is the angle formed by the slope of the TEG tracing from the r to the K value. It denotes the speed at which solid clot forms. (4) The maximum amplitude (MA) [normal range = 50–60 mm] is the greatest amplitude on the TEG trace and is a reflection of the absolute strength of the fibrin clot. It is a direct function of the maximum dynamic properties of fibrin and platelets. (5) A_{60} [normal range = MA – 5 mm] is the amplitude of the tracing 60 min after MA has been achieved. It is a measurement of clot lysis or retraction. (From Mallet and Cox[37]. Used with permission.)

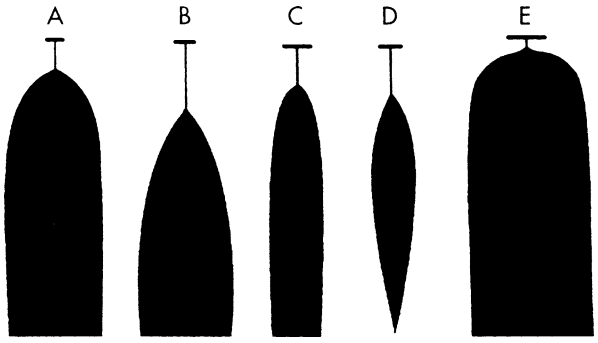

Figure 15-11. Specific hemostatic defects produce a characteristic TEG. (**a**) Normal trace. (**b**) Hemophilia: marked prolongation of *r* and *K* times; decreased α angle. (**c**) Thrombocytopenia: normal *r* and *rK* times: decreased MA (<40 mm). (**d**) Fibrinolysis. (**e**) Hypercoagulability: short *r* time; increased MA and steep clot formation rate. (a–e from Mallet and Cox[37]. Used with permission.)

whereas Fig. 15-11 shows parturients with normal as well as abnormal bleeding conditions.[37,38] Orlikowski et al. studied 49 patients with preeclampsia.[39] They found no correlation between the bleeding time and platelet count, but noticed a strong correlation between platelet count and TEG maximal amplitude (MA). Similar findings were noted by Sharma et al.[40] They noted that patients with mild preeclampsia were hypercoaguable while patients with severe preeclampsia with platelet count less than 100,000/mm^3 were hypocoaguable, and there was a strong correlation between low platelet count and MA on TEG.

The general recommendation in the past has been that regional anesthesia should be avoided if platelet count is below 100,000/mm^3 as coagulation may be abnormal if platelet counts are less than this value. Many anesthesiologists have changed their perceptions of regional anesthesia in patients with low platelet counts. At Brigham and Women's Hospital at the present time, regional anesthesia is administered in obstetric patients with platelet counts of greater than 70,000/mm^3 after due consideration of risk benefit ratio of regional versus

general anesthesia. Sharma et al.[40] found that MA does not decrease until the platelet count decreases below 70,000/mm^3. A similar conclusion was also reached by Orlikowski et al. in pre-eclamptic women. Although the safety of administering regional anesthesia with lower platelet counts as regards the risk of epidural hematoma cannot be guaranteed, nonetheless these studies do offer assistance in the risk benefit analysis when deciding between general anesthesia (airway issues) and regional anesthesia in pregnant patients with preeclampsia. Our practice is to monitor the platelet count particularly in patients with a declining trend, and place epidural catheters before the platelets decrease below the above threshold. We do not routinely request PT/PTT studies unless there is a clinical history of bleeding or other clinical condition (e.g., chronic abruption) putting the parturient at risk of abnormal studies.

Spinal Anesthesia. Previously, spinal anesthesia was contraindicated for cesarean section in parturients with severe preeclampsia. This is because of the possibility of severe hypotension in volume-contracted individuals and those receiving hypotensive medications. However, several well-conducted studies argue against this dictum.[41,42] In these studies, no differences in blood pressure were observed between spinal and epidural anesthesia while undergoing cesarean section. The requirements of ephedrine were also similar. When compared with healthy parturients, women with severe preeclampsia *developed less hypotension following spinal anesthesia*.[43] As in numerous studies in normal pregnancy, preload with crystalloid (1 L Ringers lactate) did not prevent maternal hypotension in preeclamptic patients.[44] However, changes in uterine artery velocity waveforms were minor when systolic arterial pressure was 80% or more of baseline during spinal anesthesia, and these changes did not appear to have any major effect on the clinical condition of the neonate, as assessed by Apgar score and umbilical artery pH values.[44] Therefore, maintaining systolic arterial blood pressure above 80% of baseline seems to be a reasonable approach using small amounts of ephedrine noting however, that vasopressors may have an exaggerated response in these individuals. Because of the possibility of hypotension in volume

contracted parturients with severe preeclampsia undergoing cesarean section with spinal anesthesia, there is a tendency to give a larger amount of fluid in this group of parturients. Some prefer colloid for volume expansion in parturients with severe preeclampsia.

Summary of Regional Anesthesia. Important regional anesthesia considerations are:

1. Spinal. Single shot spinal or continuous spinal anesthesia can be used. Hypotension should be treated aggressively with a small amount of ephedrine unless contraindicated.
2. Combined spinal epidural technique is preferable over one-shot spinal anesthesia if surgery is expected to be prolonged.
3. Some authors still believe that slowly titrated epidural anesthesia is associated with more stable maternal hemodynamics and hence placental perfusion. This may be the ideal anesthetic for parturients with very severe preeclampsia.
4. Blood should be drawn for a determination of the hematocrit and platelet count. Routine coagulation studies are not generally indicated. In selected cases, TEG may be helpful, if available.
5. A CVP monitor may be necessary in some cases with severe preeclampsia, for example, in the setting of refractory oliguria despite volume loading.
6. A pulmonary artery catheter is rarely required but may be considered in cases of pulmonary edema or oliguria when CVP is high.
7. Urine output should be routinely measured.
8. 2% lidocaine with epinephrine may be the drug of choice for elective cases and 3% 2-chloroprocaine can be used in emergency situations if an epidural catheter is already has been placed. 50–100 μg of fentanyl will intensify the sensory anesthesia with lidocaine.
9. Continuous fetal heart rate monitoring should be performed during induction and maintenance of regional anesthesia.
10. Postoperative analgesia may be maintained by using epidural or spinal morphine or a continuous infusion of local anesthetic and opioids.

General Anesthesia. Laryngoscopy and intubation can stimulate dangerous degrees of hypertension when performed during the usual rapid sequence induction of general anesthesia. It may be prudent to reduce blood pressure prior to induction. The hypotensive drugs that can be used for this purpose include:

1. *Labetalol* – One study showed that labetalol (1 mg/kg) will decrease the maternal blood pressure without affecting the intervillous and fetal blood flow.[45] This is the preferred agent at the present time at Brigham and Women's Hospital.
2. *Hydralazine* – It has been suggested that hydralazine can increase uterine perfusion; however, a longer time of onset makes this drug impractical for use in urgent situations.
3. *Nitroglycerin* – Nitroglycerin is a fast-acting drug but comparatively unpredictable.
4. *Nitroprusside* – Nitroprusside has a fast onset of action. *However, one should remember the remote theoretical possibility of fetal cyanide intoxication*.
5. *Calcium-channel blockers (nifedipine)* have become popular in recent years. These have the following advantageous properties: (1) they act as vasodilators, (2) they are uterine muscle relaxants, and (3) they increase renal blood flow. In severely preeclamptic parturients, nifedipine was associated with lowering of maternal blood pressure as well as prolongation of pregnancy and improvement of fetal oxygenation.[46] Recently, however, cardiovascular collapse has been reported after use of nifedipine in the presence of magnesium sulfate.
6. Intravenous opioids have also been used preoperatively to prevent reflex hypertension. Fentanyl up to 200 μg can be used intravenously prior to induction of general anesthesia.[47] Recently, remifentanil has been used as an alternative in these circumstances.[48,49]

Several problems may be encountered when using general anesthesia in parturients with severe preeclampsia.

1. Airway edema, which occasionally may result in stridor, may be encountered in these women, hence small endotracheal tubes may be necessary for intubation.
2. A hypertensive response to light general anesthesia always remains a major problem. Moore and colleagues

encountered a 50% increase in mean arterial pressure during laryngoscopy in preeclamptic women even after the preinduction use of nitroprusside.[50]

3. Drug interactions are common in this group of parturients. Magnesium sulfate can prolong neuromuscular blockade of both depolarizing and nondepolarizing muscle relaxants. Nifedipine may worsen uterine atony following delivery.

HELLP Syndrome

Weinstein originally described a symptom complex consisting of (1) hemolysis, (2) elevated liver enzyme levels, and (3) low platelet count and included this syndrome as a severe consequence of pregnancy-induced hypertension.[51] Interestingly, laboratory evidence of the HELLP syndrome may occur before the development of hypertension and proteinuria. Clinical features may include fatigue and right upper quadrant pain. Differential diagnosis of HELLP includes thrombotic thrombocytic purpura, hemolytic-uremic syndrome, and fatty liver of pregnancy (Table 15-5). Serum transaminase levels must be elevated to make the diagnosis of liver dysfunction. Anesthetic management will depend on the clotting parameters. In the case of severe thrombocytopenia, general anesthesia may be indicated; otherwise, regional anesthesia is usually the authors' choice of technique. Occasionally we have inserted

Table 15-5. Differential Diagnosis of HELLP Syndrome, Thrombotic Thrombocytic Purpura, Hemolytic-Uremic Syndrome, and Fatty Liver of Pregnancy

Disorder	HELLP	TTP	HUS	Fatty Liver of Pregnancy
Microangiopathic hemolytic anemia	+	+	+	–
Thrombocytopenic bleeding	+	+	+	+
Neurological dysfunction	+	++	±	±
Renal dysfunction	±	+	+++	+

the epidural catheter before there was a significant decrease in platelet count as described earlier provided there are no other coagulation abnormalities. Withdrawal of the catheter in the presence of thrombocytopenia is controversial. Advocates of withdrawal point to the possibility of catheter migration in the blood vessels and the risk of epidural hematoma. Opponents of withdrawal fear clot dislodgment and risk of epidural hematoma. In both situations, parturients must be followed for any signs of epidural hematoma. We often wait for the platelet counts to rise after a nadir and then consider pulling the catheter at platelet counts similar to those desired for insertion.

We report our institutional experience with thrombocytopenic parturients from all causes including those from HELLP.[52] Medical records from 1997 to 2002 of parturients with platelet counts <100,000/mm^3 during the peripartum period were reviewed for methods of anesthesia/analgesia for delivery, peripartum, and hospital course, and incidence of neurological complications; 177 patients were identified. Of these, 170 (96%) received regional anesthesia. Ninety percent of identified patients had platelet counts >70,000 / mm^3; all received regional anesthesia for either vaginal or cesarean delivery, as did all parturients with platelet counts 70,000–60,000 / mm^3 requesting regional anesthesia. In parturients with platelet counts between 50,000 and 60,000 uL, 6 received regional anesthesia and one was denied. Spinal, instead of epidural, was more often chosen in this group than in those with counts >60,000 /uL (4/6 vs. 29/160). This was likely due to two factors. First, 5 of 7 parturients in this group were presented for cesarean delivery for worsening preeclampsia without being in labor. Second, there is a some evidence of a lower risk of epidural hematoma associated with spinal anesthesia (1:220,000) vs. epidural anesthesia (1:150,000).[53] Parturients with counts <50,000 /uL received regional anesthesia only after platelet transfusion. In 82%, the platelet count was over 60,000 /uL at catheter removal.

Eclampsia

Eclampsia occurs in 0.05% of all pregnancies, and approximately 30% of seizures occur in the postpartum period in

preeclamptic mothers. Parturients remain at risk for eclampsia for at least 48 h and perhaps for as long as 1 week. Treatment of seizures should include intravenous magnesium sulfate, adequate protection of the airway, prevention of aspiration, and treatment of hypertension. Although magnesium sulfate is the drug of choice for the treatment of eclamptic seizures,[54,55] diazepam, midazolam, phenytoin, phenobarbital, and thiopental have each been used. A diagnosis of eclampsia does not contraindicate the use of epidural analgesia/anesthesia; however, we generally obtain clotting parameters prior to regional techniques. Some have advocated extra caution when performing blood patch for postdural puncture headache in the setting of postpartum preeclampsia, as injection of epidural blood can precipitate seizures by raising intracranial pressure.[56] Moreover, headache presenting in the postpartum period without a strong clinical history supporting the diagnosis of postdural puncture headache, should raise the possibility of severe postpartum preeclampsia as an alternative diagnosis.

Embolism in Pregnancy

The leading cause of maternal mortality in developed countries is embolism, three types of which have been described: thrombotic, amniotic fluid, and air.

Thromboembolism

Pregnancy is a hypercoagulable state. Parturients might be receiving low molecular weight or regular heparin for treatment or prophylaxis of deep vein thrombosis or pulmonary embolism. The challenge of LMWH is discussed in the Chapter 14.

Amniotic Fluid Embolism

The incidence of amniotic fluid embolism has been estimated from 1 in 8,000 to 1 in 80,000 pregnancies. The mortality rate is very high. Predisposing factors include advanced

maternal age, multiple gestation, macrosomic fetuses, fast labor, and intense uterine contraction following oxytocin augmentation. Clinical features include the following:

1. Occurrence usually during second stage of labor
2. Sudden chills, shivering, sweating
3. Tachypnea, cyanosis
4. Convulsions and cardiovascular collapse
5. Coagulation abnormalities (nearly universal[57]; may be the presenting sign in milder cases)

A differential diagnosis of amniotic fluid embolism includes the following:

1. Thrombotic pulmonary embolism
2. Air embolism
3. Anaphylaxis
4. Acute left ventricular failure
5. Hemorrhagic shock associated with pregnancy

Emergency cesarean section under general anesthesia is indicated in the midst of active resuscitation. Management of amniotic fluid embolism predominantly is directed to supporting the cardiovascular system. Coagulation abnormalities require substantial blood, plasma, cryoprecipitate and platelet infusions.

Venous Air Embolism

The reported incidence of maternal mortality from venous air embolism is approximately 1 in 100,000 live births. The following are possible causes of venous air embolism:

1. Traumatized vein, open uterine sinuses
2. Negative intrathoracic pressure
3. Uterine manipulation during manual extraction of the placenta and exteriorization of the uterus following cesarean section

Clinical features of venous air embolism include the following:

1. Gasping respiration
2. Chest pain
3. Ischemic ECG changes
4. Hypotension

5. Changes in heart sounds (classically, a "mill wheel" murmur; more reliably appreciated by Doppler over the maternal precordium)
6. Cyanosis
7. Cardiac arrest

Immediate treatment depends on the symptoms. If this occurs during cesarean delivery, the uterus should be placed back into the abdomen if it was exteriorized. This should be followed by flooding the field with saline. The resuscitative efforts depend on the extent of hemodynamic compromise occurring as a result of air locking in the right and atrium and ventricle. They include (1) Trendelenburg position, (2) left lateral position, (3) discontinuation of nitrous oxide and provision of 100% oxygen, (4) immediate cardiopulmonary resuscitation, and (5) a central venous catheter to aspirate air.

Although a major venous air embolism is rare during labor and delivery and cesarean section, careful attention is required, especially during the opening of the uterus for delivery as well as if the uterus is exteriorized to close the hysterotomy. A subclinical air embolism is common during cesarean delivery with exteriorization of the uterus. Forty-two episodes of VAE, defined by an increase in FEN2 of 0.1%, were detected in 97% (29/30) of patients.[58]

Fetal-Related Issues

Prematurity

The mean duration of singleton pregnancy is 40 weeks dated from the first day of the last menstrual period. "Term" gestation is defined as two standard deviations from the mean or, more precisely, 37 completed to 42 weeks of gestation. Preterm (premature) labor is defined as labor occurring prior to 37 completed weeks of gestation. Preterm birth occurs in 7–12% of all deliveries in the United States, but accounts for over 85% of all perinatal morbidity and mortality. Major problems related with prematurity include the following:

1. Respiratory distress syndrome is the major cause of mortality in premature infants. Intrapartum hypoxia and severe maternal stress during labor may increase the severity.

2. Intracranial hemorrhage is usually related to uncontrolled delivery and trauma, and neonatal hypertension that might be associated with asphyxia.
3. Ischemic cerebral damage can occur from intrapartum asphyxia, hypoxia, and hypotension.
4. There is a possibility of a prolonged effect of depressant medications because of immature metabolic and excretory systems in the preterm infant.
5. Hypoglycemia is more common.
6. Hyperbilirubinemia caused by drugs that displace bilirubin from protein-binding sites could be harmful.
7. Drug interactions can occur among tocolytic agents, corticosteroids, and anesthetic agents.

Regarding the etiology of premature labor, recent evidence suggests the presence of bacterial infection in the reproductive tract may play an important role. Epidemiologic studies have demonstrated an association of premature labor with colonization of the genital tract by group B streptococci, *Chlamydia, Neisseria gonorrhoeae*, and other organisms that cause bacterial vaginosis. Some success in preventing preterm birth has been reported in randomized trials of antibiotic treatment of bacterial vaginosis, but routine screening for asymptomatic infection has not proven successful and is not currently recommended.[59,60] Treatment of fetal fibronectin, a marker of degradation of the extracellular matrix, is often used to predict preterm delivery.[61]

Tocolytic Agent Therapy

These drugs are used to attempt stop premature contractions. Because of their side effects these agents can expose the mother and fetus to various risks. Various groups of drugs have been used for tocolysis.[62] In modern obstetric practice, long-term tocolytic therapy is no longer common, because numerous investigations have failed to show any significant prolongation of gestation or reduction in neonatal morbidity. Short-term (<48 h) use is still indicated to permit corticosteroid therapy to induce fetal lung maturation, or to allow transfer of the mother to a facility with adequate newborn intensive care resources.

Ethanol. Ethanol was one of the earliest tocolytic agents, but in the U.S. is now of only historical interest. It inhibits the secretion of antidiuretic hormone and oxytocin. Ethanol may also act directly on the myometrium and/or interfere with the action of uterine-stimulating agents such as prostaglandins. A loading dose of 7.5 mL/kg of 10% ethanol in 5% dextrose is infused over a period of 2 h. This dose is followed by a maintenance infusion of 10% ethanol at a rate of 1.5 mL/kg/h for 10 h. If labor recurs, a second or third course of ethanol is given. However, because of the major side effects and availability of better drugs, this drug has become unpopular. The possibility of maternal unconsciousness with gastric aspiration remains the major problem.

Magnesium Sulfate. Magnesium sulfate has been used as the primary tocolytic agent to prevent delivery, as an adjunct to other tocolytic agents, and also in place of other tocolytic agents when they have failed to inhibit preterm labor. Strips of myometrium excised from gravid human uteri have reduced contractility in the presence of magnesium ions. The mechanism of action is not fully understood; however, it is possible that magnesium competes with calcium for surface binding sites on the smooth muscle membrane, and also prevents an increase in free intracellular calcium that is necessary for myosin light-chain kinase activity. In addition, there is evidence that an increased magnesium ion concentration activates adenylcyclase and the synthesis of cyclic adenosine monophosphate (cAMP). This messenger increases calcium transport out of the cell as well as into the sarcoplasmic reticulum, and inactivates myosin light chain kinase, all of which decrease muscle contraction.

Anesthetic Considerations – Parturients receiving magnesium sulfate therapy are more sensitive to both depolarizing and nondepolarizing relaxants. A neuromuscular blockade monitor should be used routinely whenever relaxants are used. The minimum alveolar concentration for inhalation anesthetics is decreased in the presence of magnesium.

Calcium Channel Blockers. Although these drugs are primarily used in the treatment of ischemic heart disease and paroxysmal supraventricular tachycardia, these agents remain

potentially useful tocolytics. However, the doses necessary to inhibit preterm labor may be associated with impairment of atrioventricular conduction and hypotension. Nifedipine, because of a lower incidence of side effects, has been used for this purpose as a tocolytic agent. The contractility of myometrium is directly related to the concentration of free calcium within the cytoplasm; a decrease in the cytoplasmic free calcium level decreases contractility. Calcium channel blockers act primarily by altering the net calcium uptake through cellular membranes by blockade of the aqueous voltage-gated membrane channels selective for calcium.

Anesthetic Considerations – Parturients receiving calcium channel blockers will be more prone to the cardiovascular depressive effect of inhalational anesthetics. In addition, there may be uterine atony in the postpartum period, which is occasionally unresponsive to oxytocin and prostoglandin $F_{2\alpha}$ and this can lead to postpartum hemorrhage.

Methylxanthines. These drugs (primarily aminophylline) exhibit the action of the phosphodiesterase enzyme responsible for the intracellular catabolism of cAMP. cAMP levels increase, and this results in uterine muscle relaxation. Because of the frequent incidence of side effects and the narrow margin between therapeutic and toxic blood levels, these drugs have never became popular.

Prostaglandin Inhibitors. This class includes NSAIDs and aspirin. These drugs inhibit cyclooxygenase, which is required for synthesis of uterotonic prostaglandins. Indomethacin has been used in preterm labor with some success. The main disadvantage of this drug is the possibility of narrowing of the fetal ductus arteriosus and persistent fetal circulation. Fetal renal function may also be impaired, and transient oliguria and reversible oligohydramnios has been reported. Indomethacin has been found to be effective and safe when used for short periods (48 h) at less than 34 weeks gestation. This agent can theoretically interfere with platelet function, though no effect on the incidence of hemorrhagic complications of regional anesthesia has been documented.

β-Adrenergic Drugs. Historically the most widely used tocolytic agents, these agents act by direct stimulation of

the β-adrenergic receptors present in uterine smooth muscle, with resultant increased intracellular cAMP levels and uterine relaxation. Side effects of these drugs can be seen in both mothers and neonates, and these can be classified as follows: (1) CNS: nausea, vomiting, anxiety, and restlessness; (2) metabolic: hyperglycemia, hyperinsulinemia, hypokalemia, and acidosis; and (3) cardiovascular: tachycardia, multiple arrhythmias, decreased diastolic pressure, decreased peripheral vascular resistance, dilutional anemia, low colloidal oncotic pressure, and pulmonary edema.

Pulmonary edema is one of the most complex problems following β-mimetic therapy, and the incidence has been reported to be 1–5% in parturients.[63] The exact mechanism is unknown; however, several factors can precipitate this problem (Figs. 15-12 and 15-13):

1. Increased intravenous fluid administration
2. Multiple gestation
3. Tocolytic therapy for more than 24 h
4. Concomitant $MgSO_4$ therapy
5. Infection
6. Hypokalemia
7. Previously unrecognized heart disease

Signs of left ventricular failure are not always present, and in many instances, pulmonary fluid suggested evidence of increased capillary permeability. Multiple factors may be involved in the pathophysiology of pulmonary edema:

1. *Infection* – Certain infections can increase pulmonary capillary permeability, and this mechanism is likely the most important. Hatjis and Swain surveyed the incidence of pulmonary edema associated with infection following β-mimetic therapy. Out of 527 parturients receiving tocolysis, there was evidence of maternal infection in 52 women. The incidence of pulmonary edema was 21% (11/52), whereas it was only 1% (5 of 475) in the absence of infection.[64]
2. *Fluid Balance and Left Ventricular Dysfunction* – Cardiac output is increased during pregnancy and this can increase even further in the presence of multiple gestation. The administration of β-mimetic therapy has also been shown to increase the maternal heart rate, cardiac output, and stroke volume.[65] β-mimetic drugs can increase sodium and

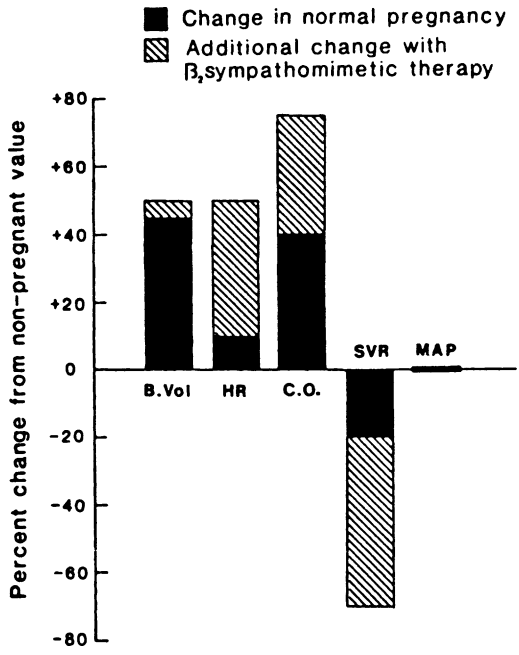

Figure 15-12. Cardiovascular changes of β-sympathomimetic therapy in pregnancy. (From Hawker[81] used with permission.)

water retention because of increased secretion of antidiuretic hormone.[64] Although all of these factors increase cardiac output, they appear only rarely to be associated with left ventricular dysfunction. Indeed, an echocardiographic study of women with beta-agonist therapy-induced pulmonary edema found normal filling pressures and no evidence of cardiac dysfunction.[66]

3. *Low Colloidal Oncotic Pressure* – In the pregnant woman colloid oncotic pressure is lower (20–25 mm Hg) than in the nonpregnant mother (28–32 mm Hg). β-mimetic therapy, because of sodium and water retention, can further lower colloid oncotic pressure and thus increase the likelihood of pulmonary edema.

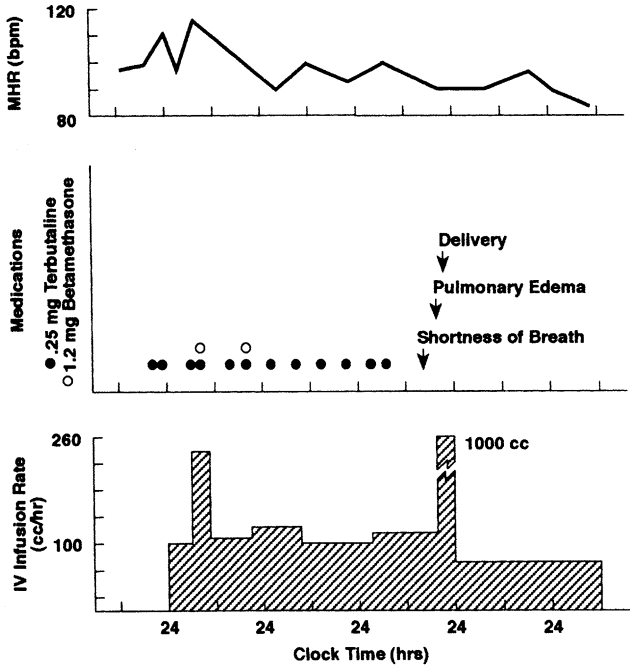

Figure 15-13. Pulmonary edema following long-term β-mimetic therapy. (Reprinted from Benedetti,[82] © 1983, with permission from Elsevier.)

Whatever the mechanism of pulmonary edema, treatment of pulmonary edema usually consists of oxygen and fluid restriction. Only rarely are diuretics such as furosemide, or mechanical ventilation and invasive monitoring necessary.

Anesthetic Management of Prematurity

Labor and Delivery. Epidural analgesia has several advantages here: (1) smaller doses of opioids or sedatives may be necessary; (2) there is better placental perfusion in the absence of hypotension, which can reduce the chance of fetal acidosis;

and (3) a well-controlled delivery may reduce the chances of intracranial hemorrhage.

Cesarean Section: Regional Anesthesia. In the presence of an unstable cardiovascular system, epidural anesthesia, because of its slower onset, may be associated with less hypotension; thus less fluid for acute volume expansion may be necessary, and less vasopressor will be needed to maintain blood pressure. Spinal anesthesia can also be used in the absence of severe maternal tachycardia. If hypotension occurs, occasionally ephedrine may not be effective in the presence of tachycardia; in this situation small doses of phenylephrine, 40 μg at a time, may be necessary to maintain the blood pressure. Volume expansion should be carefully regulated; O_2 saturation monitoring and continuous urine output monitoring are prudent. In the presence of refractory pulmonary edema, use of CVP or pulmonary artery lines may be necessary.

General Anesthesia. The following list includes points to keep in mind when using general anesthesia:

1. *Small endotracheal tubes may be necessary in the presence of vocal cord edema (this can happen if the parturient is kept in a head-down position to stop premature labor).*
2. Inhalation anesthetics should be used carefully in the presence of calcium channel blockers.
3. *$MgSO_4$ therapy can interact with both depolarizing and nondepolarizing muscle relaxants.*
4. Parturients receiving β-mimetic tocolytics for more than 24 h should have their electrolyte levels checked. Hypokalemia can cause cardiac arrhythmias, and hyperventilation can worsen the situation. Hyperglycemia may require treatment.
5. Halothane (seldom used now) is contraindicated in the presence of β-mimetic drugs because of the possibility of cardiac arrhythmias.
6. Tocolytic drugs are associated with uterine muscle relaxation and atony and can cause uterine hemorrhage.
7. Volume expansion should be modest in the setting of beta adrenergic therapy.
8. Active neonatal resuscitation may be necessary.

Postmaturity

Post-dates pregnancy is defined as gestation beyond 42 weeks (294 days after the last menstrual period). However, many of the risks of postmaturity may be seen even at 40 or 41 weeks. Major problems encountered in postmaturity include the following:

1. Reduced uteroplacental blood flow causing fetal distress.
2. Umbilical cord compression can occur as a result of oligohydramnios with an increased incidence of fetal distress.
3. Meconium staining of amniotic fluid is common.
4. Higher incidence of macrosomia and shoulder dystocia.[67]

Anesthetic Management of Postmaturity

Labor and Delivery. Epidural analgesia is associated with several advantages: (1) relief of labor pain, decreased endogenous catecholamine release, and thus increased uteroplacental perfusion; and (2) it can be used for cesarean in the event of fetal distress. However, continuous close monitoring of the fetal heart rate is mandatory, and hypotension must be prevented.

Cesarean Section. Epidural or spinal anesthesia can be used provided that hypotension is prevented. General anesthesia may be used in the presence of fetal distress if all the precautions mentioned before are observed.

Breech Presentation

Breech presentation was once commonly managed by vaginal delivery. However, evidence from a large, randomized, multinational study showed better neonatal outcomes with elective cesarean delivery.[68] For this reason, cesarean delivery for breech presentation is the most common management. Unless it is an emergency situation like a prolapsed cord, where general anesthesia may be necessary, spinal or epidural anesthesia can be utilized in elective situations. For labor and delivery, epidural analgesia can be used to facilitate vaginal delivery.

Multiple Gestations

Twins

For labor and delivery, continuous epidural analgesia offers the better approach. This method obviates the use of depressant drugs like opioids or sedatives and also allows a controlled delivery over a relaxed perineum. In addition, occasionally second twin distress complicates twin vaginal delivery, and presence of epidural analgesia allows rapid extension of the block for emergency cesarean delivery. Nitroglycerin in small doses can also be used for uterine relaxation to facilitate version or extraction, especially for the second baby. If there is no epidural analgesia, general anesthesia is occasionally needed for version or extraction, especially for the second baby. For cesarean delivery, spinal or epidural anesthesia can be used if there is no contraindication. For emergent situations, like cord prolapse, general anesthesia should be used.

Triplets or Quadruplets

The abdominal route is usually the mode of delivery. Major problems include the following:

1. More profound aortocaval compression and a higher incidence of hypotension are observed.
2. There is an increased tendency toward hypoxemia because of the upward displacement of the diaphragm.
3. In the presence of a grossly enlarged uterus, gastric emptying may be theoretically compromised beyond that of normal pregnancy, thereby increasing the risk of aspiration in these individuals.
4. Fetuses in multiple gestations are often premature and may have growth restriction.

Anesthetic Management

Epidural anesthesia may be preferred because of a lower incidence of hypotension, possibly less possibility of high neuraxial anesthesia (due to excessive lumbar lordosis and flattened thoracic kyphosis), and less time pressure for the completion of surgery.

Spinal anesthesia may be used, but the incidences of hypotension may be higher. Judicial volume replacement and use of vasopressors are mandatory. If there are more than 3 babies one should preferably avoid spinal anesthesia. CSE may allow both the convenience and rapid onset of spinal anesthesia with smaller amounts of local anesthetic and the ability to extend the duration of the anesthetic. A well-conducted general anesthesia may also be used, particularly for higher order gestations.

Fetal Distress (Nonreassuring Fetal Status)

The etiology of fetal distress is associated with maternal causes, placental causes, and fetal problems. The American College of Obstetricians and Gynecologists prefers the term *nonreassuring fetal status*, as the incidence of false positive fetal heart rate patterns is very high.

Maternal Causes

Maternal factors that may be responsible for fetal distress include maternal systemic disease, e.g., diabetes, chronic hypertension, drug abuse (cocaine), as well as physiological problems such as supine hypotensive syndrome or other cardiovascular or pulmonary problems.

Placental Causes

Decreased placental perfusion because of preeclampsia, diabetes, postmaturity, or placental abruption, can give rise to fetal distress. Umbilical cord problems such as a prolapsed cord should also be considered in this category.

Fetal Causes

Inherent congenital anatomic as well as other abnormalities will also increase the chances of fetal distress.

Diagnosis

Obstetric diagnostic tools have very low positive predictive value and are discussed in the chapter on Fetal Monitoring. The fetal heart rate tracing remains the hallmark of fetal assessment, but ultrasound, amniocentesis, and in some centers fetal capillary pH measurement ("scalp pH") are sometimes used.

Anesthetic Management

Anesthetic management should include the following points:

1. *Avoidance of aortocaval compression by left uterine displacement should be the first step* in any situation where there is a suspicion of fetal distress.
2. Oxygen supplementation is customary. The fetus normally exists at an almost vertical portion of its oxygen dissociation curve; hence a small change in fetal oxygen tension can result in some change in oxygen content and delivery of the oxygen in the fetus (see Table 15-6). However, there is now considerable controversy as to how beneficial maternal oxygen therapy is, at least in nonemergency situations. Because it is otherwise a low risk intervention, it is reasonable to apply oxygen to the mother when the fetus is compromised.
3. Treatment of hypotension becomes a hallmark in the restoration of placental circulation if there is a decrease in blood pressure for any reason. Although both ephedrine and phenylephrine are used in elective situations, we prefer

Table 15-6. Effect of Umbilical Arterial Oxygen Tension with Varying Maternal Inspired Oxygen Concentration

Maternal FIO_2	Maternal PaO_2 (mm Hg)	Umbilical Artery PaO_2 (mm Hg)
0.21	96	15
0.47	232	19
0.74	312	21
1.0	423	25

ephedrine as the first-line drug in cases of nonreassuring fetal status unless contraindicated.
4. Oxytocin therapy is generally discontinued, but the obstetric team usually makes this decision.
5. In a few situations, the administration of tocolytic drugs like terbutaline can be used to relax the uterus and increase placental circulation. This treatment is also decided by the obstetrician.
6. Amnioinfusion has been tried for the treatment of variable deceleration or thick meconium.
7. Epidural anesthesia can increase placental perfusion, especially in parturients in labor, provided that the maternal blood pressure is kept close to normal levels. The block can be rapidly extended if cesarean or instrumental vaginal delivery is necessary.
8. In the case of acute fetal distress, the anesthetic management for cesarean section may include (1) epidural 2-chloroprocaine or 1.5–2% lidocaine with epinephrine, either combined with bicarbonate (1 in 10 mL, 8.4 mEq) if time permits; avoidance of hypotension is extremely important; (2) general anesthesia with proper precautions; or (3) spinal anesthesia, depending on the anesthesiologist. Even in urgent situations, we prefer spinal anesthesia by the most experienced practitioner available, because it appears to be associated with better 1 minute Apgar scores.[69] Aggressive neonatal resuscitation may be necessary, and pediatricians should be present at delivery whenever possible.

Intrauterine Fetal Death

The major causes of intrauterine fetal death[70] are as follows:
1. Chromosomal abnormalities
2. Congenital malformations, e.g., heart defects, urinary tract anomalies
3. Multiple gestation
4. Infection
5. Placental factors, e.g., abruptio placenta, vasa previa, subchorial hemorrhage, placenta previa, placental insufficiency due to diabetes, preeclampsia, postdate pregnancy
6. Cord accidents

7. Maternal immunological diseases
8. Maternal thyroid disease
9. Isoimmunization
10. Maternal trauma

Before making an anesthetic decision, the anesthesiologist must find the associated maternal problems that might have caused the fetal demise. Epidural analgesia offers adequate pain relief for labor and delivery. However, anesthesiologists must examine the clotting parameters before using regional anesthesia in these cases because of the possibility of coagulation problems (abruptio placentae). Pritchard observed disseminated intravascular coagulation in mothers where dead fetuses stayed in the mother for more than 1 month[71] regardless of the etiology; hypofibrinogenemia was a common finding. Expectant management of fetal demise for this long is rare in modern practice. Pregnant women with abnormal clotting parameters may need intravenous labor analgesia. Coagulation abnormalities can be corrected appropriately using fresh frozen plasma or cryoprecipitate that contains high concentrations of factor VIII, and fibrinogen.

Transfusion-Related Issues (Newer Transfusion Protocols)

When treating acute hemorrhage in parturients, some guidelines for blood component therapy include:

1. One unit of platelets (suspended in 20–70 mL of plasma) may raise the platelet count by 10,000/mm^3.
2. Fresh frozen plasma (FFP), 1 unit (250 mL), contains 200–400 mg of fibrinogen and may raise plasma fibrinogen content by 10 mg/100 mL. FFP also contains various clotting factors excluding platelets.
3. Cryoprecipitate (1 unit = 15–20 mL) contains almost as much fibrinogen as 1 unit (250 mL) of FFP.

At Brigham and Women's Hospital, we have recently changed our approach to management of obstetric hemorrhage. If a major blood loss is suspected, we initiate transfusion of blood and plasma transfusion at a 1:1 ratio prior to any laboratory studies. This is based on the experience of

hemorrhage management in trauma patients, and in patients with ruptured abdominal aortic aneurysm. The latter study suggested that proactive administration of platelets and FFP improve coagulation competence, reduces postoperative hemorrhage, and increases survival in massively bleeding ruptured abdominal aortic aneurysm patients.[72] The former study is from evaluation of the Trauma Research Database.[73] The authors analyzed the ICU outcome with early INR. The survival outcome was related to ICU admission INR. Although the data are retrospective, this prompted authors to recommend aggressive resuscitation protocol of FFP:RBC ratio of 1:1. Similar data has emerged from recent experience in military trauma. This management protocol of FFP:RBC ratio of 1:1 is being implemented in several centers to correct coagulopathy aggressively, and early. Prospective studies are necessary, however, because survivorship bias may complicate retrospective studies. Patients living long enough during major hemorrhage to receive FFP may appear to have better outcomes than those who died before FFP becomes available.

Recombinant Factor VIIa

From the published evidence it would appear that rFVIIa is gaining acceptance as a novel haemostatic agent following obstetric hemorrhage as well as in parturients with clotting factor deficiencies.[74,75] It is a potent thrombin generating, haemostatic drug. Recent evidence suggests that the supranormal levels of rFVIIa administered clinically causes a thrombin burst following the generation of a prothrombinase complex, on the surface of activated platelets. This can occur not only in the absence of factors VIII and IX (explaining its efficacy in hemophilia patients), but also in the presence of thrombocytopenia or platelet dysfunction. However, fibrinogen is required for this factor to be efficacious. The usual dose range varies from 20 to 90 μg/kg. Two recent retrospective series report 80–90% success in controlling postpartum hemorrhage following the use of rFVIIa.[76,77] The downside of rFVIIa use is the occurrence of strokes due to embolic phenomena and therefore this factor has to be used cautiously.[77] Factor VIIa is also extremely expensive. Prospective studies are currently in progress.

Summary

There is a need for further studies on anesthetic needs for high-risk parturients. Successful anesthesia will depend on technical skills and understanding of maternal and fetal physiology, pathophysiology of the pregnancy induced complication, and the pharmacology of different drugs and their interactions with the anesthetic techniques.

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16
Non-delivery Obstetric Procedures

Cervical Cerclage

Cervical incompetence complicates up to 1% of all pregnancies. It is characterized by premature dilation of the internal cervical os and shortening of the cervix from the internal os to the uterine cavity. It is associated with early pregnancy loss and premature birth. Cervical cerclage is a procedure performed at least 23,000 times annually in the United States.[1]

There are three techniques in use at the present time: McDonald transvaginal approach, Shirodkar transvaginal approach, and the abdominal cerclage. The first two techniques are technically easier and much more popular. All cerclage procedures involve a circumferential suture or band tied around the cervical os to strengthen and support the cervix and prevent further dilation. The McDonald technique is simpler and is simply a purse-string suture placed in the neck of the cervix as high

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in the vagina as possible. The Shirodkar involves dissection of the bladder and rectum away from the anterior and posterior aspects of the cervix to allow a imbedded band to be placed higher on the cervix, closer to the internal os. The abdominal approach allows an even higher placement of the suture but requires an abdominal incision both at placement and removal, and is reserved for cases of extreme cervical scarring or other pathology.

The effectiveness of cerclage in preventing early pregnancy loss or preterm delivery is questionable. One large multicenter randomized trial found a 25% decrease in delivery before 34 weeks (13% vs. 17%) and very low birthweight infants (10% vs. 13%).[2] Other trials have failed to find any advantage of cervical cerclage in women with cervical incompetence detected on examination or by ultrasound.[3,4]

Anesthetic Options

Both regional and general anesthesia techniques are acceptable choices for placement of a cervical cerclage.[5] As with most pregnant patients, at Brigham and Women's Hospital we usually favor regional anesthesia. Cerclage placement is usually performed as an outpatient at 16–24 weeks' gestation, which affects the choice of anesthetic. A Shirodkar takes somewhat longer than a McDonald, but both should generally require less than 30–45 min of surgical anesthesia. Postoperatively, patients are monitored for signs of uterine activity as well as anesthetic recovery before discharge.

Regional Anesthesia

At Brigham and Women's Hospital, we prefer short-duration spinal anesthesia for most cases. Hyperbaric mepivacaine 45–60 mg, lidocaine 45–50 mg, procaine 100 mg, or bupivacaine 7.5–10 mg will provide adequate coverage and duration for the procedure. *Some anesthesiologists no longer favor lidocaine due to its association with Transient Neurologic Symptoms (TNS) following ambulatory spinal anesthesia in the lithotomy position*, but pregnant patients may be at lower risk of this

complication during cerclage placement.[6] A level at least to T10 is required to ensure coverage of the cervix. Because there is little visceral stimulation, opioids are not as important as during intra-abdominal cases, but fentanyl 10–20 μg may be added to deepen the block and reduce the total dose of local anesthetic required (e.g., 30 mg lidocaine or 5.25 mg bupivacaine[6]). Low-dose epidural analgesia has also been reported for cervical cerclage.[7]

General Anesthesia

General anesthesia is an appropriate and safe choice for properly fasted patients who do not desire regional anesthesia or in whom it is contraindicated.[5] Induction with propofol and fentanyl and maintenance with a volatile anesthetic, alone or with nitrous oxide, is a reasonable regimen. *Whether the airway must be secured with an endotracheal tube is a matter of controversy. Otherwise healthy, fasted pregnant women in the first or second trimester are probably not at increased risk for aspiration (see Chapter 1). Therefore, we believe it is acceptable to use spontaneous breathing by mask or laryngeal mask airway during maintenance.* If endotracheal intubation is performed, succinylcholine is used to facilitate the procedure, but neuromuscular blockade is not necessary during the operation. Intubation is indicated in emergency cases or when spontaneous breathing or maintenance of a patent airway may be difficult (e.g., morbid obesity).

Cerclage Removal

Cerclage removal can usually be done without anesthesia, frequently as an outpatient as the parturient approaches term gestation. Occasionally, due to patient discomfort or growth of granulation tissue around the knot in the cerclage suture, anesthesia is required for removal. If the patient will be remaining in the hospital for labor, an attractive option is to place an epidural for the cerclage removal and leave it in place without infusing further local anesthetics until the patient is in active labor. Lidocaine 2% (with or without epinephrine), 10 ml, will

often suffice for cerclage removal. Alternatively, CSE with short-acting local anesthetic may be employed. If the procedure is to be performed as an outpatient with expectant management until the patient enters labor spontaneously, anesthetic options include short-duration spinal anesthesia (e.g., lidocaine or mepivacaine, 30 mg) or intravenous sedation. The latter should be considered only in fasted, non-laboring patients with no additional risk factors for aspiration.

Dilation and Evacuation (D&E)

Dilation of the cervix for evacuation of the uterine contents may be required in a number of circumstances. Most commonly, D&E is used in cases of first-trimester incomplete, inevitable, or missed abortion. Occasionally, a postpartum patient experiencing hemorrhage due to retained products of conception (i.e., placental fragments or membranes) will require the procedure. In many cases in obstetrics, the procedure will be done on an emergency basis.

The procedure is performed in the lithotomy position. After aseptic preparation of the perineum, a weighted speculum is placed in the vagina to expose the cervix. We prefer that a paracervical block be performed by the obstetrician (Fig. 16-1). Typically 1% chloroprocaine is injected to achieve rapid onset of anesthesia with a low chance of systemic toxicity due to absorption or unintentional intravascular injection. In first-trimester cases, dilation of the cervix with progressively larger dilators is performed next; in most postpartum cases this step can be omitted. Suction curettage (evacuation) is performed to remove the intrauterine contents. In postpartum cases, this is usually accomplished under ultrasound guidance to reduce the chance of uterine perforation, which complicates approximately 5% of such cases.

Anesthetic Options

The procedure may be performed in an operating room or in a less fully-equipped procedure room. In either case, standard monitors and resuscitation equipment should be immediately

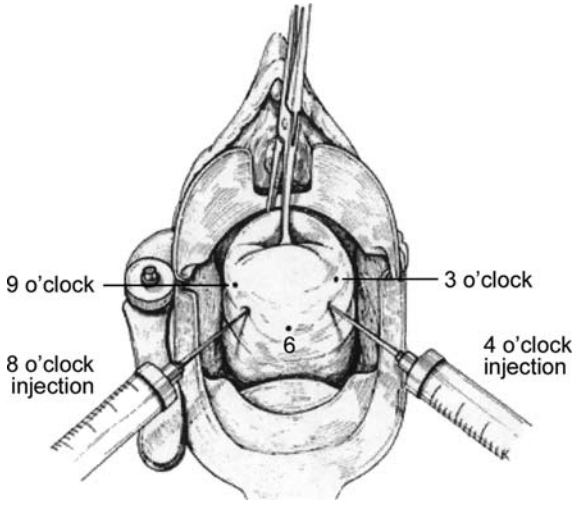

Figure 16–1. Technique for paracervical block. Anesthetic, typically 1% chloroprocaine, is injected laterally at the 4- and 8-o'clock positions of the cervix. (From Shulman and Ling.[20] Used with permission.)

available. At Brigham and Women's, we prefer that cases of postpartum hemorrhage be treated in the OR in case more extensive intervention is required. A standard history and physical examination is performed, with particular attention to the severity of bleeding or hemodynamic compromise and the interval since the last oral intake. In cases of stable patients in the first or second trimester who have been NPO for at least 6–8 h we prefer intravenous sedation combined with paracervical block. Routine monitors are applied and an IV secured. Intravenous midazolam (1–2 mg) and fentanyl (50–100 μg), followed by small boluses of propofol (10–20 mg/min) are usually sufficient. Unless the patient is actively bleeding heavily, we favor ketorolac, 30 mg IV, at the end of the procedure, to help control postoperative pain from uterine cramps. If a more extensive procedure is contemplated, either general endotracheal anesthesia or spinal anesthesia is an appropriate choice.

Postpartum patients with in situ epidural catheters can undergo the procedure under epidural analgesia. The block can be extended if necessary with 2% lidocaine with epinephrine or 3% chloroprocaine, 5–10 ml to achieve a T10 sensory level and dense sacral anesthesia. *Postpartum patients without epidural analgesia pose a dilemma. Although the procedure is likely to be short and uncomplicated, most anesthesiologists consider women in the immediate postpartum period to be at risk for aspiration, irrespective of the time since last oral intake. We generally favor short-acting spinal anesthesia in these cases (e.g., lidocaine or mepivacaine, 30–45 mg).*

Postpartum Tubal Ligation

Timing of Tubal Ligation

Many obstetricians prefer to perform postpartum tubal ligation immediately after the delivery or before the women are discharged from the hospital. This procedure has a few *distinct advantages:*

1. Immediately after delivery, the uterine fundus lies between the umbilicus and symphysis pubis, so the fallopian tubes remain easily accessible via a periumbilical mini-laparotomy incision
2. Uncomplicated postpartum sterilization does not increase the length of the hospital stay.
3. There is less medical cost.

On the other hand, one can find a *few disadvantages* in performing this procedure immediately after delivery:

1. The physiological changes of pregnancy do not revert back to normal for at least 6 weeks.
2. Tubal ligation is an elective procedure.[8] Anesthetizing women at higher risk of aspiration (with a "full stomach") for elective surgery is controversial.
3. Success of the procedure may be less and patient may regret her decision more frequently than interval procedures performed 6 or more weeks postpartum.[9]
4. Performing postpartum tubal ligation may be a resource drain in busy obstetric units, particularly outside normal hours, and should not prevent anesthesiologists from providing more urgent obstetrical services, including labor analgesia.[10]

Physiologic Changes of Pregnancy in the Postpartum Period

Many physiologic changes of pregnancy (see Chapter 1) persist in the immediate postpartum period, when tubal ligation is performed. The principal change of interest to anesthesiologists relates to gastric acidity and motility. Classically, *a gastric volume of more than 25 mL and a pH of less 2.5 is considered "at risk" for aspiration.*[11] Using these criteria, there is controversy regarding whether women are more frequently at risk in the first postpartum day. Blouw compared gastric volume and pH between parturients undergoing tubal ligation 8 h postpartum vs. nonpregnant women having laparoscopic tubal ligation. Thirty-three percent of the postpartum women and 64% of the control women were found to be at risk.[12] James et al. compared three groups of postpartum women undergoing tubal ligation at 1–8 h, 9–23 h, and 24 h or more hours, and nonpregnant controls. There were no differences in the proportion of women who were at risk among any of the groups. Sixty percent of the women were at risk. Conversely, an ultrasound study found 40% of postpartum women had solid food particles in their stomachs when presenting for tubal ligation. In an experimental study, the same group found 95% of postpartum women fed a standard meal had solid food in the stomach at 4 h, compared to 19% in nonpregnant volunteers.[13] Therefore, most anesthesiologists consider postpartum women to be at risk for aspiration. It is not clear what the optimal time after delivery for tubal ligation should be. *At Brigham and Women's Hospital we urge the obstetric team to encourage women to have epidural anesthesia for labor and delivery if they are contemplating postpartum tubal ligation.*

Anesthetic Techniques

Epidural Anesthesia

An in-situ epidural catheter used for labor analgesia can usually be reactivated to provide surgical anesthesia for the procedure. An observational study demonstrated >90% success up to 24 h after delivery, but a decline in successful reactivation after 24 h.[14] However, epidural reactivation is more time consuming, and a failed attempt at reactivation even more

so, compared to elective spinal anesthesia.[15] The choice of drug and dose should take into account the heightened sensitivity to local anesthetics in pregnancy. However, there is controversy regarding the duration of this increased sensitivity after delivery. A sensory level to at least T5–6 is necessary when performing postpartum tubal ligation to prevent discomfort from peritoneal traction. There are no comparative trials of different local anesthetic solutions for tubal ligation. We prefer 2% lidocaine with epinephrine, with or without fentanyl 50–100 μg. 2-Chloroprocaine 3% and plain lidocaine are reasonable alternatives.

Spinal Anesthesia

As with epidural anesthesia, less local anesthetic is required in parturients than in nonpregnant women when a subarachnoid block is performed (Fig. 16-2). This decreased requirement does not reach prepregnant values for at least 24 h.[16] The usual precautions and preparations for spinal anesthesia, including

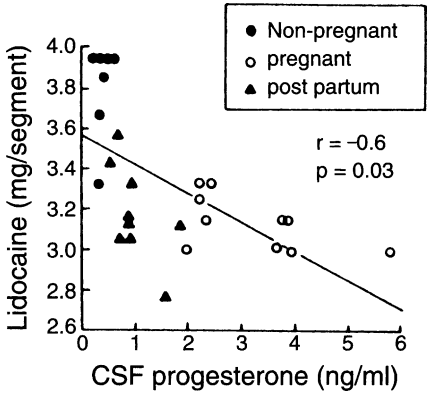

Figure 16–2. Correlation between cerebrospinal fluid (*CSF*) progesterone (ng/mL) and lidocaine (milligrams per segment) in nonpregnant patients, parturients having cesarean section, and patients 24 h after delivery. (Adapted from Datta et al.[16])

consideration of aspiration prophylaxis, fluid loading, routine monitoring, are indicated. Hyperbaric local anesthetic is used to ensure a midthoracic level of anesthesia. Bupivacaine (9–12 mg) or lidocaine or mepivacaine (45–60 mg) are suitable choices. These doses are similar to those used for cesarean section, though the shorter duration of the procedure allows a modest reduction in dose. Fentanyl 10 μg added to local anesthetic can intensify the sensory anesthesia. Because of the possibility of TNS, use of lidocaine has been controversial. However, the incidence of TNS in pregnant and immediate postpartum patients is low.[17] Recently in response to the declining popularity of lidocaine spinal anesthesia we have also employed mepivacaine, in doses similar to lidocaine, with success as noted above for cervical cerclage. Some centers have used intrathecal meperidine (1 mg/kg) for postpartum tubal ligation. The duration of surgical anesthesia was observed to be 30–60 min and the duration of postoperative analgesia was over 6 h.[18]

General Anesthesia

At Brigham and Women's Hospital we try to avoid general anesthesia for postpartum tubal ligation. If general anesthesia is necessary, one should be aware of the reduction in the minimum alveolar concentration in parturients; again it is not known how long this reduction in the minimum alveolar concentration lasts following delivery. As discussed, it is prudent to consider the postpartum patient to be at risk for aspiration irrespective of the fasting interval preceding the procedure.

The techniques for general anesthesia for postpartum tubal ligation are as follows:

1. Intravenous line and routine monitors, careful preoxygenation
2. Metoclopramide, 10 mg intravenously (unless contraindicated), plus nonparticulate antacid
3. Rapid-sequence induction with thiopental, propofol, or ketamine plus succinylcholine, and endotracheal intubation
4. Ventilation with O_2 alone or with N_2O and a low concentration of inhalation anesthetics (to prevent uterine relaxation and bleeding)

5. Neuromuscular blockade after induction is not always required but a short-acting agent is preferred.
6. Opioids (fentanyl, morphine, or hydromorphone)
7. Some authorities advocate routine decompression of the stomach via orogastric tube
8. Oxytocin for maintenance of uterine tone may counteract relaxing effects of volatile anesthetics.

Postoperative Pain Relief

Tubal ligation is usually a painful procedure. Hence, adequate postoperative pain relief is important. Small doses of intrathecal or epidural morphine have been used in a few centers. Others have used infiltration of bupivacaine of the tubes and infiltration of local anesthetic in the wound, combined with parenteral ketorolac, with success.[19] Intravenous, intramuscular, or oral opioids are also useful for postoperative pain relief.

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Anesthesia for Nonobstetric Surgery During Pregnancy

It has been estimated that every year in the United States about 50,000 pregnant women (0.5–2.2%) will receive anesthesia for various surgical indications during their pregnancy. The purpose of this surgery may be (1) to prolong gestation, (2) unrelated to the pregnancy, or (3) to correct fetal anomalies. Hence, an understanding of the effects of different anesthetic drugs and techniques on the mother and fetus is essential to the safe administration of anesthesia to pregnant women undergoing surgery. Recently, a question of preoperative pregnancy testing in adolescents has been raised. The authors observed retrospectively 412 adolescent women undergoing surgery. The overall incidence of a positive test was 1.2%. The authors concluded that mandatory pregnancy testing is advisable in all adolescent surgical candidates aged 15 years and older.[1] However, compulsory pregnancy testing is not practiced in all hospitals; a

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hospital policy should be established after a discussion with the obstetric as well as anesthesia divisions.

Ideal anesthetic consideration for pregnant women undergoing surgery should include maternal safety, fetal well-being, and continuation of pregnancy.

Maternal Safety

A thorough understanding of physiological changes during pregnancy is very important. This has been discussed in Chapter 1. The most important points will be reiterated here.

I. Respiratory system changes
   A. Capillary engorgement of respiratory mucous membrane
   B. Increased minute ventilation due mainly to an increase in tidal volume and to a lesser extent to an increase in respiratory rate
   C. Decreased end-tidal CO_2 and arterial CO_2 and decreased arterial to end-tidal CO_2 difference
   D. Decreased functional residual capacity
   E. Increased oxygen demand
II. Cardiovascular system changes
   A. Increased cardiac output
   B. Increased blood volume
   C. Aortocaval compression from the gravid uterus
III. Gastrointestinal system changes
   A. Decreased lower gastroesophageal sphincter pressure
IV. Central and peripheral nervous system changes
   A. Decreased anesthetic requirement both for general, epidural, and spinal anesthesia

Fetal Well-Being

Avoidance of the teratogenic effects of anesthetics on the fetus is paramount in the care of pregnant women undergoing nonobstetric surgery. One should also try to avoid derangement of fetal homeostasis, which can be affected directly and indirectly by anesthetic drugs and techniques.

The teratogenic effect of anesthetic drugs is a very controversial issue that has no clear-cut answer. Exposure to anesthetic agents may be either acute during surgery – sedatives, hypnotics, narcotics, muscle relaxants, local anesthetics, oxygen and carbon dioxide, or inhalational anesthetics – or chronic because of occupational exposure to inhalational anesthetics.

Acute Exposure to Anesthetics

Even though human studies of the effect of acute exposure of anesthetics demonstrated an increased incidence of spontaneous abortion, they failed to show any teratogenic effects on the fetus.[1–5] In 1986 Duncan and colleagues retrospectively reviewed the incidence of congenital anomalies and spontaneous abortions in 2,565 pregnant women who underwent surgery.[6] These women were matched with a control group consisting of a similar number of pregnant women with similar maternal ages as well as areas of residence. *No significant differences in the rate of congenital anomalies were observed between the study and control groups. However, there was a significant increase in spontaneous abortions in women who underwent surgery during their first and second trimesters. One of the drawbacks of this study was that the vast majority of surgeries were performed with the woman under general anesthesia, so one could not differentiate the effect of regional or general anesthesia on the incidence of spontaneous abortion.* Mazze and Kallen retrospectively analyzed pregnant women from Swedish health care registries (1973–1981).[7] Out of 720,000 cases, 5,405 underwent surgery. The incidence of congenital malformation was not different between the group that underwent surgery and the one that did not; however, there was a slightly higher incidence of prematurity and intrauterine growth retardation in the group that had surgery. The authors did not observe any association of this adverse outcome with the anesthetic used or the operation the woman underwent.

Chronic Exposure to Anesthetics

Several reports of increased congenital anomalies as well as spontaneous abortions among anesthesiologists and other operating room personnel have been published.[8,9] An important

report regarding this issue was published by an ad hoc committee of the American Society of Anesthesiologists.[10] They found an increased risk of congenital anomalies and spontaneous abortions in women working in operating room areas when compared with non-operating room female hospital employees. In a separate study, an increased rate of spontaneous abortions was reported among female dentists and assistants who used inhalational anesthetics as compared with those who used local anesthetics in their practice.[11,12] On the other hand, in a different study, Ericson and Kallen were unable to demonstrate an increased risk of adverse fetal outcome in operating room or anesthesia nurses as compared with a control group of medical floor nurses.[13]

Until now, no causal relationship has been proved between the chronic exposure to inhalational anesthetics and fetal anomalies. However, the importance of the scavenging system has been stressed in the operating room environment. Rowland et al. observed the effect of nitrous oxide on pregnancy in 459 dental assistants and divided them into five groups: (1) unexposed, (2) low scavenged, (3) high scavenged, (4) low unscavenged, and (5) high unscavenged. The mean time to conception was significantly higher in the high unscavenged group.[14]

Effect of Anesthetics on the Fetus

Teratogenic studies of different anesthetic agents have been studied mainly in animals. It is very difficult as well as impractical to extrapolate these results to humans. Fortunately, no commonly used anesthetics, when given acutely are known teratogens. Subtle effects on the fetal brain are the subject of intense investigations at present.

Sedative and Hypnotic Agents

Barbiturates have been used in humans as induction agents for many years. Although there is a conflicting report in animals regarding the teratogenic effect of barbiturates, in pregnant women these agents have been found to be safe.[15] Phenothiazines have also been observed to be without any

adverse effect in humans.[16] The association of minor tranquilizers with teratogenicity is controversial, although retrospective studies have shown diazepam and chlordiazepoxide to be associated with congenital malformations.[17,18] On the other hand, more recent studies did not find any increased risk of congenital anomalies following use of diazepam.[19] Midazolam has not been observed with any teratogenicity. Recently published literature on women attempting to commit suicide during pregnancy by taking large doses of drugs such as diazepam, medazepam, promethazine, and meprobamate did not show that these drugs were fetotoxic.[20–22]

Opioids

Geber and Schramm observed the teratogenicity of a wide variety of narcotics administered to pregnant hamsters at critical periods of fetal central nervous system development.[23] Comparative studies using single or multiple doses showed increased fetal anomalies with diacetylmorphine, thebaine, pentazocine, morphine, hydromorphone, as well as meperidine. On the other hand, other authors observed that the chronic administration of morphine, fentanyl, sufentanil, or alfentanil in pregnant rats was not associated with any teratogenic effect.[24–26] There is also no evidence that these opioids are associated with teratogenicity in humans.

Muscle Relaxants

There is no evidence of an adverse effect in fetal development following the use of muscle relaxants.

Local Anesthetics

In a very large study by the Collaborative Perinatal Project, and in other studies, no evidence of teratogenicity was found in pregnant rats following the administration of benzocaine, procaine, tetracaine, or lidocaine.[27–29] *In contrast, the use of cocaine is associated with fetal congenital malformations both in humans and animals.*[30] *This may be explained by cocaine-mediated vasoconstriction and, hence, fetal tissue hypoxia.*

Oxygen and Carbon Dioxide

Hypoxia as well as hypercarbia have been associated with teratogenicity in animal species.[31,32] Although a high concentration of inspired oxygen at atmospheric pressure does not produce any adverse effects,[33] hyperbaric oxygen exposure is associated with fetal anomalies in animals.[34]

Inhalation Anesthetics

The addition of inhalational anesthetics such as nitrous oxide or halogenated agents to oxygen has become a routine practice when administering general anesthesia. Some of these agents have been implicated in the development of fetal anomalies as well as in premature births.

Nitrous Oxide. Interest in the teratogenic effect of nitrous oxide has grown significantly among anesthesiologists since Nunn and colleagues observed the effect of the short-term nitrous oxide anesthetic administration on plasma concentrations of methionine, tryptophan, phenylalanine, and *S*-adenosylmethionine in humans.[35] The authors observed a 15% reduction in tryptophan concentration after exposure to 60–70% nitrous oxide for a mean duration of 88 min. The plasma methionine concentration decreased significantly following exposure to 50% nitrous oxide for up to 11 days in rats.[36] Using nitrous oxide during surgery and up to 24 h postoperatively, Skacel and colleagues observed a significant decrease in the plasma methionine concentration following major vascular surgery in humans.[37] Recovery took place following discontinuation of nitrous oxide administration. The main reason for the decreased plasma methionine concentration is related to inhibition of enzyme methionine synthetase.[35] Thus the teratogenic effect of nitrous oxide may be related to the interference with DNA synthesis by altering folate metabolism[35] (Fig. 17-1). Keeling and colleagues observed the effect of pretreatment with folinic acid on the teratogenic effect of nitrous oxide in rats.[38] Major skeletal abnormalities in the group receiving nitrous oxide without pretreatment increased five times as compared with the control group, whereas the group that was pretreated with folinic acid was not significantly

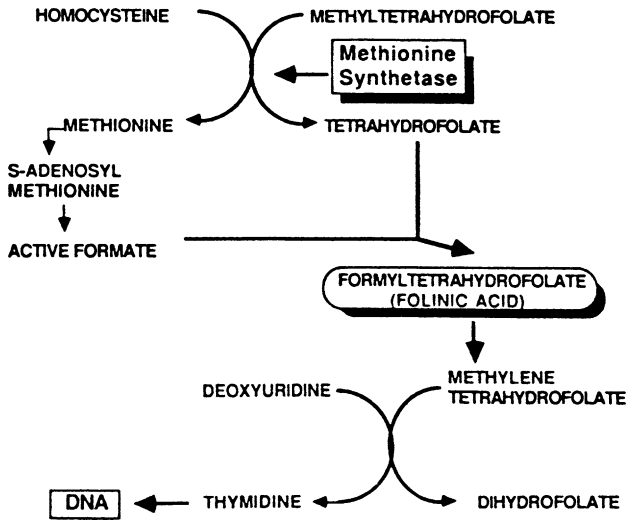

Figure 17–1. Mechanisms of the interference of nitrous oxide in DNA synthesis. Nitrous oxide directly blocks the transmethylation reaction by which methionine is synthesized from homocysteine and methyltetrahydrofolate. Nitrous oxide oxidizes vitamin B_{12}, the cofactor of the enzyme methionine synthetase. (From Levinson and Shnider.[55] Used with permission.)

different from controls. Mazze et al. also observed teratogenicity in rats after exposure to 50% or more of nitrous oxide for 24 h on day 8 of pregnancy.[39] Interestingly, the teratogenic effect was prevented by the addition of fentanyl or halogenated anesthetics with nitrous oxide.[40,41] Hence the authors concluded that the mechanism of teratogenicity following nitrous oxide exposure may not be related to interference in DNA synthesis but rather to a physiological effect of nitrous oxide, such as reduction in uterine blood flow due to increased sympathetic activity.[41] However, when an α-antagonist like phenoxybenzamine was used, the investigators could not completely abolish the teratogenic effect of nitrous oxide.[42] In summary, although in rats there is a relationship between the use of nitrous oxide

and teratogenicity, the exact mechanism is not clear at the present time. In humans, short exposures to nitrous oxide during the second trimester were not associated with any adverse effect.[43]

Halogenated Anesthetics. Halothane, enflurane, and isoflurane at physiological minimum alveolar concentrations are not associated with any teratogenicity in rats,[41] nor has evidence of teratogenicity been seen in humans with these agents.[19] The newer inhalational agents desflurane and sevoflurane are also not associated with any teratogenicity.[44]

Effects on the Fetal Brain: Behavioral Teratogenicity

The brain continues to develop throughout gestation and after birth.[45] Enduring change in behavior without obvious structural abnormalities has been termed behavioral teratogenicity. It is believed that compounds that interact with NMDA (*N*-methyl-D-aspartate) and GABA (gamma aminobutyric acid) receptors can trigger programmed cell death, or apoptosis, in developing brain.[45] Although apoptosis is a normal part of embryogenesis, some animal experiments have demonstrated functional or behavioral abnormalities accompanying an increase in cell death, such as impaired maze learning. These changes may persist at least into young adult life.[46] Because many anesthetic agents are NMDA antagonists or potentiators of GABA transmission, it is conceivable that anesthetic exposure during brain development could lead to neurodegeneration.

In a study of neonatal rats, Jovtovic-Todorovic et al.[46] observed significant increases in staining for apoptosis throughout the brain when the rats were exposed to 6 h of midazolam, N_2O, and isoflurane anesthesia at 7 days of age (which corresponds to the peak of synaptogenesis in the rat, a period likely to span many weeks from midgestation to the postnatal period in humans). The authors, however, used doses that produce a surgical plane of anesthesia in the rat, which were substantially larger than those commonly employed in humans. They also observed evidence of impaired synaptic function in the

hippocampus, important for memory formation. Studies in animals allowed to mature into young adulthood showed impaired learning in various maze tests, compared to air- and vehicle-treated controls. Subsequent investigations by these and other laboratories have demonstrated similar results with other anesthetics, including ketamine and propofol, in both anesthetic and even subanesthetic doses.[45,47,48] Guinea pigs exposed to isoflurane -nitrous oxide -midazonlam for 4 h in utero also demonstrated increased apoptosis and neuronal cell loss throughout the brain.[48] There is even some preliminary data in non-human primates that GABA-mimetic agents can induce apoptosis in developing brain.[47]

As with all non-human animal studies, extrapolation is difficult to determine the degree of risk anesthetics pose to humans undergoing general anesthesia, or fetuses exposed in utero to maternal anesthesia. Hopefully, in future, a better understanding of the mechanism of toxicity will also point to strategies to block the harmful effects. While laboratory and eventual clinical investigations proceed, it is prudent to assume that general anesthetics are potentially toxic to the developing fetal brain, and their use in obstetric anesthesia should continue to be a rare event reserved for emergencies.

Continuation of the Pregnancy

Surgery during pregnancy is associated with a higher incidence of premature labor and spontaneous abortion. The incidence is higher in lower abdominal, pelvic, and cervical surgery. Tocolytic drugs, both for prophylactic and therapeutic reasons, are used quite often to prevent premature delivery.

Recommendations for Minimizing Chances of Abortion or Premature Labor

Elective surgery should be postponed until after delivery. In semielective cases, it is best if surgery can be postponed until after the first trimester. In emergency cases, the anesthetic of choice should depend on the site and extent of the

surgery to be performed. If possible, regional anesthesia, e.g., spinal, epidural, or nerve block, is advisable. However, general anesthesia can be administered if necessary.

Preoperative medications, if necessary, may include benzodiazepines and opioids. Routine, nonparticulate antacid should be used, and rapid-sequence induction is often selected. *Although there is no general consensus, it is reasonable to use an endotracheal tube for longer or more extensive procedures.* Depending on the duration of surgery, one can use either depolarizing or nondepolarizing muscle relaxants. Anesthesia can be maintained with nitrous oxide, oxygen, and halogenated anesthetics. Morphine, fentanyl, sufentanil, or alfentanil can be used as analgesics. *Hyperventilation should always be avoided because it can reduce uteroplacental perfusion as well as shift the maternal hemoglobin dissociation curve to the left.*

For regional anesthesia, maintenance of normal blood pressure is absolutely necessary, and the routine use of oxygen by face mask is recommended. *Whether general or regional anesthesia has been chosen, left uterine displacement from the mid second trimester onward is mandatory.*

Routine monitoring should include blood pressure, electrocardiogram, oxygen saturation, capnograph, and temperature. In addition, fetal heart rate monitoring, if possible, should be performed from 24 weeks onward. Close communication between the anesthesiologist and obstetrician regarding fetal heart rate monitoring is necessary as well as interpretation of the tracings. Because most of the medications used for general anesthesia can abolish the fetal heart rate variability, the baseline fetal heart rate should be the main indicator of fetal well-being during general anesthesia. Depending upon the location of surgery, tocodynamometry can be used to monitor uterine contractions. This obviously becomes routine in the postoperative period when treating pregnant women with preterm contractions with tocolytics.

Recently, laparoscopic surgery during pregnancy has been used with success. One must have a basic knowledge of physiological changes during pregnancy. During laparoscopic cholecystectomy, women are placed in a head-up position during dissection and in a head-down position for irrigation. In parturients, these positions may have significant cardiovascular

and respiratory effects. Peritoneal insufflation pressure should be kept low because of the possibility of aortocaval compression. Ventilation should be optimal to maintain end-tidal PCO_2 at 32–34 mmHg. Bhavani Shankar et al. prospectively evaluated the $PaCO_2$–$ETCO_2$ difference in eight parturients undergoing laparoscopic cholecystectomy with CO_2 pneumoperitoneum. The intra-abdominal pressures were maintained around 15 mmHg. These women underwent surgery with general anesthesia during the second and third trimester of their pregnancies. Adjusting minute ventilation to maintain the $ETCO_2$ at 32 mmHg, the arterial blood gases (alpha-stat method) were measured at fixed surgical phases: preinsufflation, during insufflation, postinsufflation, and after completion of surgery.

We found no significant differences in either mean $PaCO_2$–$ETCO_2$ gradient or $PaCO_2$ and pH during the various phases of laparoscopy. During the surgical phase (i.e., preinsufflation, insufflation, and postinsufflation), the maximal $PaCO_2$–$ETCO_2$ difference detected was 3.1 mmHg (range, 1.1–3.1 mmHg). It appears that $ETCO_2$ correlates well with arterial CO_2, and adjusting ventilation to maintain $ETCO_2$ also maintains optimal maternal arterial CO_2.[49,50] We also showed that cardiac output decreases by about 30% during laparoscopy surgery in pregnant subjects and therefore vasopressors (ephedrine) should be administered to maintain blood pressures within 20% of the baseline.[51]

Intrauterine Surgery

Intrauterine surgery is becoming popular for treating fetal congenital anamolies.[52–55] In the majority of cases the pregnancy is continued, whereas for the ex-utero intrapartum treatment (EXIT) surgery is performed on the fetus on placental support followed by delivery (Fig. 17-2). Maternal and fetal considerations for anesthetic implications have already been discussed. The minimum alveolar concentration for halothane has been observed to be 50% lower in the fetal lamb as compared with the pregnant ewe (0.33% vol. vs. 0.69% vol, so the fetus will be anesthetized if the mother is)[52]. In case of EXIT

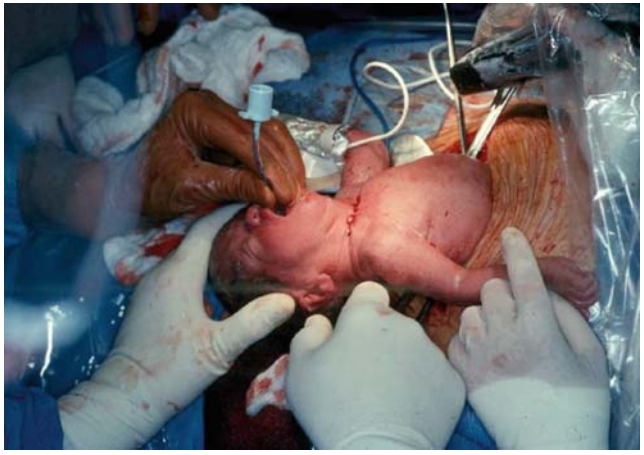

Figure 17–2. A fetus with a neck tumor. Airway being secured before disrupting uteroplacental–umbilical cord blood flow.

procedure, uterine relaxation is also important to prevent uterine contraction and separation of placenta. This is achieved by 1.5–2.0 MAC inhalational agents. Ephedrine or phenylephrine is used for maintenance of baseline blood pressure to maintain uteroplacental blood flow. Following delivery of the infant, inhalation anesthetic should be discontinued and use of uterotonic drugs is mandatory.

In intrauterine surgery, fetal movements are to be avoided. This can be accomplished by administering anesthetics and opioids to the mother, which will ultimately reach the fetus via the placenta in varying concentrations. Epidural or combined spinal-epidural can also be used for the surgery, and uterine relaxation can be achieved with nitroglycerin. Muscle relaxants and opioids can be directly administered to the fetus. Pancuronium maintains better fetal cardiovascular stability than does curare; vecuronium can also be used.[53] To prevent hypothermia of the fetus, the operating room should be kept as warm as possible and the uterus should be irrigated with a warm solution. Fetal monitoring will depend on the surgery and will vary from continuous fetal heart rate monitoring to

pulse oximetry and transcutaneous electrode measurement of blood pH and PO_2 if a body part is accessible.

Following surgery, monitoring of the fetal heart rate and uterine contractions should be routine because of the possibility of the onset of premature labor. Tocolytic drugs like magnesium sulfate are used for the prevention of preterm labor following discontinuation of the inhalation anesthetic at the conclusion of the surgery. For postoperative pain relief, patient-controlled intravenous analgesia can be used. If an epidural catheter is present, use of epidural morphine will be ideal.

Recently, percutaneous fetal aortic valve and pulmonary valve dilatations are being performed for hypoplastic ventricles via ultrasound guidance. These procedures can be performed under general or regional anesthesia. If general anesthesia is contemplated, the authors do not generally use more than 1 MAC of inhalational agent as uterine relaxation is not preferred in this approach. It is preferred that the fetus does not change positions as a result of uterine relaxation. Fetal analgesia and paralysis is provided by ultrasound-guided fetal intramuscular injections of fentanyl (30 μg) and vecuronium. Maternal depth of anesthesia is monitored via BIS. Maintenance of maternal paralysis is necessary to avoid unexpected maternal movements. An additional advantage of not using excessive maternal inhalational agents is that it avoids undue hypotension, and thus maintains uteroplacental blood flow. The recovery of the mother is quick and minimal postoperative analgesia is required.[54]

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18
Assisted Reproductive Technology

Assisted reproductive technology (ART) includes in vitro fertilization-embryo transfer (IVF-ET), gamete intrafallopian transfer (GIFT), zygote intrafallopian transfer (ZIFT), tubal embryo transfer (TET), and frozen embryo transfer (FET). These techniques also apply to oocyte donation and gestational carriers. In vitro fertilization technique (IVF) involves obtaining mature oocytes from ovarian follicles (egg retrieval, ER) and incubating them with sperm. The embryos are then transferred into the uterine cavity. Since Steptoe and Edwards, of England, performed the first successful IVF,[1] significant strides have been made in our understanding of scientific principles underlying this technique. This has enabled many women to conceive where the conventional methods have failed. In the United States, the use of IVF techniques has resulted in 52,041 neonates in 2005 alone.[2] However, IVF technology has generated substantial ethical and moral debates around the world. It has also resulted in certain complications of gestation that were unlikely in the past, such as octuplet pregnancy.

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In Vitro Fertilization Process

Each menstrual cycle is associated with a single preovulatory oocyte. However, hormonal stimulation can increase this number, facilitating retrieval of multiple oocytes per cycle. Statistically, this increases the probability of a live birth. To begin, ovarian down-regulation is achieved with the administration of a gonadotropin-releasing hormone agonist (GnRH-a) such as Lupron. This induces pituitary and ovarian suppression. The ovarian down-regulation minimizes the formation of single dominant follicle or the onset of premature ovulation. Following down-regulation, ovarian hyperstimulation is achieved with follicular stimulating hormone (FSH) and human menopausal gonadotropin (HMG). The result is followed by ultrasonographic confirmation of follicular growth and a progressive increase in serum estrogen levels.

Once follicular maturity is reached, ovulation is induced by human chorionic gonadotropin hormone. This process generates approximately 10–15 oocytes. Occasionally there are as many as 70 oocytes. Using ultrasound guidance, all visible follicles are aspirated with each follicle generally containing a single oocyte. The oocytes are placed in an organ culture dish containing the sperm, insemination medium, and fetal serum. The fertilization process takes approximately 16–20 h after insemination. The transfer of the fertilized egg is performed when the embryo reaches the four- to eight-cell stage via a transfer catheter into the uterine cavity vaginally. The transfer of the embryos is usually performed 2–3 days after fertilization (cleavage stage) or 5–6 days after fertilization (blastocyst stage). Occasionally, in the presence of normal fallopian tubes, the mixture of oocytes and liquefied semen is directly introduced into the tubes by laparoscopy (gamete intrafallopian transfer). Rarely, the fertilized oocytes (two distinct pronuclei stage) are transferred through a catheter into the distal portion of the fallopian tube laparoscopically (zygote intrafallopian transfer). After hormonal stimulation, the pituitary function may be insufficient to provide adequate hormonal support to growing corpus luteum. This necessitates administration of parenteral progesterone until the results of pregnancy tests are known, or completion of the first trimester.

Effect of Anesthetics on IVF Process

Most oocyte retrieval procedures are performed via the ultrasonographic transvaginal approach and rarely by the laparoscopic technique. Transvaginal approach of egg retrieval is associated with pain and the majority of these procedures require anesthesia, whereas vaginal embryo transfer to the uterus is a painless procedure and does not usually require anesthesia. Shatford and colleagues assessed pain associated with transvaginal ultrasonography-guided oocyte recovery in 164 women.[3] The intensity of pain was assessed from the McGill pain questionnaire. Seventy-eight percent of women assessed visual analogue scale (VAS) to be 5 or less (a reasonably tolerable level of discomfort), and 6% of the participants scored the pain as 7 or more (relatively intense pain) immediately after the procedure; however, the pain intensity decreased significantly after 1 hour of the procedure. All women in this study received opioids 1 h prior to the procedure and a paracervical block with 14 mL of 0.5% lidocaine at the time of surgery.

Most transvaginal oocyte retrieval procedures can be performed under intravenous propofol (continuous or intermittent injections) with opioid supplements with the patient breathing spontaneously. On the other hand, GIFT and ZIFT procedures involve laparoscopy and thus require general endotracheal anesthesia.

Propofol and Thiopentone

Most animal and human trials support the view that propofol has minimal effect on the fertilization process in clinically used dose ranges.[4–8] There is a dose-dependent accumulation of propofol in the follicular fluid.[9,10] However, it is unclear from the literature as to what concentration of propofol affects the fertilization process. The available studies do not demonstrate correlation between the reproductive outcome measures and the follicular fluid concentration of propofol in the ranges studied.[9–11] There is also no difference in the outcome measures between general anesthesia administered with propofol (oxygen/air) and paracervical block administered by mepivacaine

for ER procedures.[8] Furthermore, no adverse reproductive effects were observed when propofol (2.7 mg/kg) was compared with thiopentone (5 mg/kg) for induction of general anesthesia in patients undergoing GIFT procedures.[6] However, when propofol concentration is higher (40 times higher than those detected clinically), it can result in DNA damage as studied in hamsters.[12] There is also conflicting data for ZIFT procedures administered with propofol. There was a lower incidence of ongoing pregnancies when propofol-nitrous oxide anesthesia was used as compared to thiopentone-nitrous oxide-isoflurane anesthesia.[13] Hence, further studies are required to elucidate the effects of propofol on the reproductive process. It seems reasonable to infer, however, from the available studies so far, that propofol seems to be a reasonable drug of choice for transvaginal ER procedures.

Thiopentone can be detected in follicular fluid as early as 11 min after administration of general anesthesia in patients undergoing GIFT procedures. However, this did not have any significant effect on the pregnancy rates as compared to propofol.[14]

Nitrous Oxide

It is well known that nitrous oxide decreases methionine synthetase activity, and DNA synthesis in animals and humans.[15,16] Nitrous oxide also impairs the function of mitotic spindle in cell cultures.[17] Despite these findings, clinical studies using nitrous oxide for laparoscopic GIFT and ZIFT procedures did not find any significant difference in the outcome when compared to those where nitrous oxide was not used.[5,18]

Inhalational Anesthetic Agents

Halogenated volatile agents may affect IVF outcomes in two ways. First, there is evidence that these agents depress DNA synthesis and mitosis in cell cultures.[19,20] Isoflurane adversely affects embryo development in vitro,[21,22] particularly in higher concentrations (3%). The timing of administration of isoflurane is also critical. Development of the embryo was impaired

only when isoflurane was administered within four hours of predicted onset of cleavage.[22] *However, there is some controversy about interpolating animal embryonic studies to human embryos*. There is some evidence to the effect of volatile agents in human clinical studies on reproductive outcomes. Lower pregnancy rates have been reported when halothane was used as compared to enflurane for ET and GIFT procedures.[23,24]

Secondly, inhalational agents can also increase prolactin levels, and increased prolactin levels have been associated with decreased oocyte development and uterine receptivity. Critchlow et al.[23] observed increases in plasma prolactin levels with enflurane in nitrous oxide/oxygen technique for GIFT procedures. However, these changes did not occur 4–10 min after induction and did not affect follicular fluid prolactin levels or fertilization rates.

Despite all the evidence of inhalational agents affecting embryo development, when reproductive outcome measures are analyzed in some clinical studies there is evidence to the contrary. Lewin and colleagues compared the oocyte recovery rate and the fertilization rate in two groups of women.[25] In one group, ten women had follicular aspiration during laparoscopy under general anesthesia. In the second group, ten women had ultrasonically guided follicular aspiration with local anesthetic. A volume of 10–15 mL of 0.5% bupivacaine hydrochloride was used for local infiltration, and sedation was provided with intravenous infusion of meperidine 1.5 mg/kg, and diazepam 10 mg, in normal saline administered intravenously during the procedure. They did not observe any difference in either the oocyte recovery or the fertilization rate.

Presently, there is no data to support or deny the use of newer inhalational agents such as sevoflurane and desflurane.

Local Anesthetic Agents

Local anesthetic agents (chloroprocaine and lidocaine) have been shown to affect both fertilization and embryo development.[26,27] Bupivacaine produces adverse effects only at higher concentrations.[27] Despite these in vitro findings, Wikland et al. reported no decreases in fertilization and clinical pregnancy rates in patients who received a modified paracervical block

with lidocaine for transvaginal ER.[28] Favorable pregnancy rates have also been reported after GIFT procedures performed under epidural lidocaine anesthesia.[29]

Opioids, Benzodiazepines, and Ketamine

Animal and human trials have shown that meperidine, fentanyl, and alfentanil do not interfere with fertilization and embryo development.[21,30] Follicle concentration of these drugs is extremely low. The only exception seems to be morphine. Morphine has been to shown to decrease the fertilization capability in sea urchins.[31]

Midazolam did not impair fertilization and embryo development in vivo and in vitro even when administered in doses of 500 times than used clinically.[32] Midazolam has not been detected in follicular fluid when administered in small bolus or infusion doses for anxiolysis and sedation for IVF procedures.[33,34] Furthermore, a midazolam (0.06 mg/kg) and ketamine (0.75 mg/kg) combination was comparable to general anesthesia with isoflurane in reproductive outcome measures for IVF procedures.[35]

Antiemetic Agents

Metoclopramide induces hyperprolactinemia with subsequent impairment of ovarian follicle maturation and corpus luteum function.[36] However, when given as a single dose immediately prior to oocyte retrieval, it is unlikely to have significance on the mature oocyte. It may be prudent to avoid repeated doses to prevent increases in prolactin. This is because higher pregnancy rates have been associated with decreased levels of prolactin.[36,37]

Anesthetic Techniques for Ultrasound-Guided Transvaginal Oocyte Retrieval

From the ongoing discussion, it is obvious that there is some controversy regarding the effect of anesthetic agents on fertilization and embryonic development.[38] There are many nonanesthetic dominant factors that may have a greater influence

in deciding the final outcome of IVF procedures. It is conceivable that anesthetics may play a miniscule role in the overall success of IVF technology. *From the available data, opioids, midazolam and propofol, in moderate doses, seem to be a reasonable choice for IVF procedures.* General anesthesia is preferred for transvaginal ER procedures since the procedure is short and the women can be discharged quicker, compared to spinal anesthesia. Propofol is used for intravenous general anesthesia either by intermittent injection or continuous infusion. Fentanyl (50–100 μg) is used routinely, and some anesthesiologists also use midazolam (2 mg). Women are allowed to breathe spontaneously via a high-flow oxygen mask and ventilation is monitored via a capnograph. If airway problems are anticipated with the above technique, a laryngeal mask airway may be used. On rare occasions, particularly in very obese individuals, endotracheal anesthesia with propofol, succinylcholine, and inhalational agents can be used. The percutaneous abdominal approach of ER may require anesthesia using LMA or endotracheal intubation as warranted by the circumstances of the case.

If general anesthesia is contraindicated, spinal anesthesia can be used for the ER procedure. Lidocaine 45 mg (1.5% hyperbaric) mixed with 10 μg of fentanyl or lidocaine 30 mg (1.5% hyperbaric) mixed with 25 μg of fentanyl is commonly used. One can avoid intravenous opioids and sedatives. In a study by Tsen et al., 3 mg of hyperbaric bupivacaine was compared with 30 mg (1.5%) lidocaine mixed with 25 mcg of fentanyl. A longer duration for voiding was observed in the bupivacaine group.[39]

General anesthesia is used for GIFT and ZIFT techniques as these involve a laparoscopic approach. The technique is similar to any conventional laparoscopic procedure and consists of the following steps:

1. A small amount of nondepolarizing muscle relaxant is used to prevent fasciculation from succinylcholine.
2. Induction of anesthesia can be initiated with propofol.
3. Intubation is performed following succinylcholine administration.
4. Relaxation is maintained by using either a succinylcholine infusion (0.1%) or nondepolarizing muscle relaxants depending on the anticipated duration of the procedure.

5. Anesthesia is maintained with inhalational agent in oxygen/air.
6. Small amounts of intravenous opioids are administered.
7. Neuromuscular block is reversed at the conclusion of the procedure if nondepolarizing muscle relaxants have been used.

In the future, improvements in fiberoptic methods of oocyte retrieval and fallopian tube cannulation could potentially avoid invasive laparoscopic interventions. Recent improvements in fiberoptic technology have allowed mini laparoscopic procedures to be performed for GIFT procedures. These advances may minimize the anesthetic requirements and thus decrease the effects of anesthetics on the fertilization and embryonic development.[40]

Complications of IVF Procedure

Ovarian Hyperstimulation Syndrome (OHSS)

OHSS affects up to 10% of women who go through the IVF process. In most cases the condition is mild, but some women get a severe form of OHSS. The risk factors include age less than 35 years and very high estrogen levels while undergoing fertility treatments. The characteristic changes in OHSS cycles include increases in the levels of thrombin-antithrombin III and plasmin-α_2 antiplasmin complexes in the plasma and shortened activated partial thromboplastin time.[41] In a milder form of OHSS, women may complain of mild abdominal discomfort, whereas severe OHSS is characterized by the presence of intraperitoneal fluid, pleural effusion, hypotension, and oliguria. Clinical findings may consist of fluid and electrolyte imbalance, torsion of the ovarian cyst as well as thromboembolic phenomenon.

Other Complications

The success rate of in vitro fertilization at the present time is in the range of 40–45% according to the Society of Assisted Reproductive Technologies. IVF procedures can be associated with some major pregnancy-related problems that contribute

to fetal mortality[42]: The Society for Assisted Reproductive Technology has set forth some guidelines on the number of embryos transferred during in vitro fertilization process to reduce the number of high-order multiple pregnancies.[43] *The number of embryos transferred depends on the maternal age, previous failed cycles, quality of embryos, and the mode of insertion of embryos (ET or ZIFT)*. In addition to multiple pregnancies, other complications that can occur are:

1. Premature labor with fetal loss
2. Ectopic pregnancies
3. Vaginal bleeding
4. Congenital abnormalities
5. Pregnancy-induced hypertension

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19
Maternal Mortality and Morbidity

Maternal mortality and serious morbidity from obstetric anesthesia are rare. Although this is reassuring, important lessons can still be learned to continue to reduce the incidence toward zero. Moreover, changing demographics of the obstetric population are likely to challenge obstetric anesthesiologists to maintain the impressive safety record they have attained. Assisted reproductive technologies have allowed older women and those with major coexisting disease to bear children. Obesity is increasing to epidemic levels. Improved medical care of women with congenital heart disease and other previously fatal conditions has allowed them to reach childbearing age and conceive.

Information on maternal mortality comes from several sources. For a half century, triennial confidential inquiries into maternal mortality in England and Wales have been published, and these represent the best information available on the incidence and causes of this tragic event, because record keeping is mandated at the national level.[1] In the United States, three reports based on reviews of death certificates and some associated medical records have appeared.[2–4] These provide valuable insights but are likely not as complete as the UK registry. Finally, the American Society of Anesthesiologists Closed Claims Project periodically reviews cases leading to malpractice suits.[5] Although this represents only a subset of all maternal injuries (i.e., those resulting in a lawsuit), patterns of injuries and death can still be gleaned.

The reports of Confidential Enquiries into Maternal Deaths (CEMD; now the Confidential Enquiry into Maternal and Child Health, CEMACH) as well as US audits show a changing pattern in overall obstetric mortality and mortality due to obstetric anesthesia. In the 1950s, approximately 1/42,000 women died

S. Datta et al., *Obstetric Anesthesia Handbook*,
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of aspiration in labor and delivery.[6] In the last 20 years, however, only 2 cases of aspiration appeared in the ASA Closed Claims registry.[5] Similarly, in the 1980s, failed endotracheal intubation was the most common anesthetic-related cause of maternal mortality.[2] But in the most recent CEMACH report, covering 2003–2005, there were six anesthesia-related deaths, but none related to loss of the airway at induction.[1] The same result was found in a US study of maternal mortality in Michigan from 1985 to 2003; there were eight anesthesia-related maternal deaths but none due to airway problems during induction.[4] Increased use of regional anesthesia, awareness of the elevated risk of difficult intubation in obstetrics, and improved emergency airway algorithms, including rescue use of the laryngeal mask airway, are credited with this marked improvement.[2] Indeed, the risk of maternal death from anesthesia was more than 16 times higher in general vs. regional anesthesia in a US nationwide death certificate study.[2]

The CEMACH and Michigan reports, however, do sound a note of caution for management of the airway *after emergence from anesthesia*. In the CEMACH report, three deaths were due to airway loss in morbidly obese patients in the postpartum period, two after general and one after spinal anesthesia. In the Michigan study, five deaths due to airway loss postoperatively were reported. These results suggest that vigilance regarding the obstetric airway must continue into the postoperative period, and that when appropriate, enhanced monitoring may be indicated.

Overall causes of maternal mortality (excluding anesthetic-related causes) are illustrated in Fig. 19-1. Death from complications of preeclampsia have declined over the last two decades, and thromboembolism has generally increased. Death from hemorrhage and amniotic fluid embolism have remained approximately steady. Anesthesia-related death remains a rare cause compared to these major obstetric etiologies. A US survey of 1.5 million births from 2000 to 2006 showed the major causes to be similar, though the order was different: preeclampsia > amniotic fluid embolism > hemorrhage > cardiac disease > thromboembolism.[7] In both sources, death was more common in the setting of cesarean delivery than vaginal delivery.

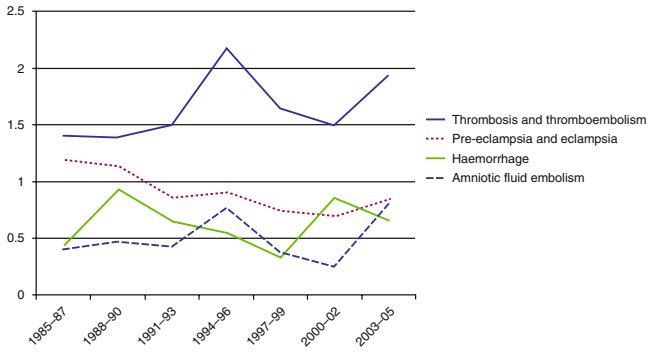

Figure 19–1. Causes of maternal mortality reported by the triennial reports of the Confidential Enquiries into Maternal and Child Health. (Data from Lewis.[10])

Besides mortality, serious maternal morbidity should also be recognized. The ASA Closed Claims experience has been reported twice in the last two decades for obstetric-related cases.[5,8] The more recent report shows some major developments when comparing claims before and after 1990. A far smaller fraction was related to airway and aspiration problems, and more were related to nerve injury; more were related to regional vs. general anesthesia; fewer represented substandard care; and fewer resulted in payment. Figure 19-2 shows the relative frequency of claims for various causes before and after 1990. The greatest payments were made in cases of maternal death, maternal brain damage, and neonatal brain damage. In neonatal brain injury cases, poor communication between the obstetrical care team and the anesthesiologist and delay in anesthesia care were associated with contribution to the injury by anesthesia care.[5]

In conclusion, anesthesia care contributes only modestly to maternal mortality and anesthesiologists have achieved an impressive reduction in mortality and major morbidity due to anesthesia care. Challenges remain, however, and the changing face of the obstetrical population and obstetric care will continue to require searching for even safer techniques.[9]

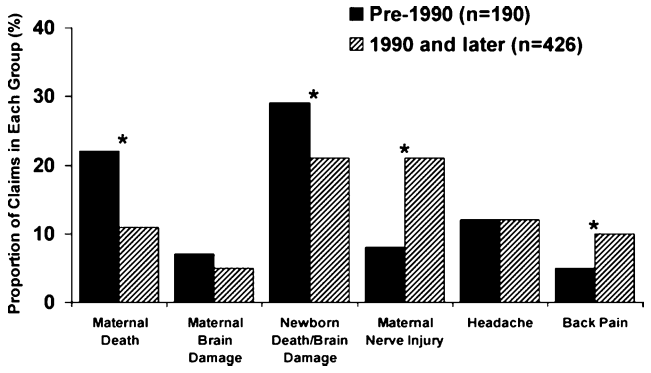

Figure 19–2. Proportion of claims made in the ASA Closed Claims database before and after 1990. (From Davies et al.[5] Used with permission from Lippincott Williams and Wilkins.)

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Appendix A Guidelines for Regional Anesthesia in Obstetrics

These guidelines apply to the use of regional anesthesia or analgesia in which local anesthetics are administered to the parturient during labor and delivery. They are intended to encourage quality patient care but cannot guarantee any specific patient outcome. Because the availability of anesthesia resources may vary, members are responsible for interpreting and establishing the guidelines for their own institutions and practices. These guidelines are subject to revision from time to time as warranted by the evolution of technology and practice.

19.1 GUIDELINE I

Regional anesthesia should be initiated and maintained only in locations in which appropriate resuscitation equipment and drugs are immediately available to manage procedurally related problems.

Resuscitation equipment should include, but is not limited to: sources of oxygen and suction, equipment to maintain an airway and perform endotracheal intubation, a means to provide positive pressure ventilation, and drugs and equipment for cardiopulmonary resuscitation.

19.2 GUIDELINE II

Regional anesthesia should be initiated by a physician with appropriate privileges and maintained by or under the medical direction[1] of such an individual.

Committee of Origin: Obstetrical Anesthesia (Approved by the ASA House of Delegates on October 12, 1988, and last amended on October 17, 2007)

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Physicians should be approved through the institutional credentialing process to initiate and direct the maintenance of obstetric anesthesia and to manage procedurally related complications.

19.3 GUIDELINE III

Regional anesthesia should not be administered until: (1) the patient has been examined by a qualified individual[2]; and (2) a physician with obstetrical privileges to perform operative vaginal or cesarean delivery, who has knowledge of the maternal and fetal status and the progress of labor and who approves the initiation of labor anesthesia, is readily available to supervise the labor and manage any obstetric complications that may arise.

Under circumstances defined by department protocol, qualified personnel may perform the initial pelvic examination. The physician responsible for the patient's obstetrical care should be informed of her status so that a decision can be made regarding present risk and further management.[2]

19.4 GUIDELINE IV

An intravenous infusion should be established before the initiation of regional anesthesia and maintained throughout the duration of the regional anesthetic.

19.5 GUIDELINE V

Regional anesthesia for labor and/or vaginal delivery requires that the parturient's vital signs and the fetal heart rate be monitored and documented by a qualified individual. Additional monitoring appropriate to the clinical condition of the parturient and the fetus should be employed when indicated. when extensive regional blockade is administered for complicated vaginal delivery, the standards for basic anesthetic monitoring[3] should be applied.

19.6 GUIDELINE VI

Regional anesthesia for cesarean delivery requires that the standards for basic anesthetic monitoring[3] be applied and that a physician with privileges in obstetrics be immediately available.

19.7 GUIDELINE VII

Qualified personnel, other than the anesthesiologist attending the mother, should be immediately available to assume responsibility for resuscitation of the newborn.[3]~The primary responsibility of the anesthesiologist is to provide care to the mother. If the anesthesiologist is also requested to provide brief assistance in the care of the newborn, the benefit to the child must be compared to the risk to the mother.

19.8 GUIDELINE VIII

A physician with appropriate privileges should remain readily available during the regional anesthetic to manage anesthetic complications until the patient's postanesthesia condition is satisfactory and stable.

19.9 GUIDELINE IX

All patients recovering from regional anesthesia should receive appropriate postanesthesia care. following cesarean delivery and/or extensive regional blockade, the standards for postanesthesia care[4] should be applied.

19.10 GUIDELINE X

There should be a policy to assure the availability in the facility of a physician to manage complications and to provide cardiopulmonary resuscitation for patients receiving postanesthesia care.

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19.11 References

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4. Standards for Postanesthesia Care (Approved by ASA House of Delegates 10/12/88 and last amended 10/27/04).

Appendix B

Practice Guidelines for Obstetric Anesthesia

An Updated Report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia[1]

Practice guidelines are systematically developed recommendations that assist the practitioner and patient in making decisions about health care. These recommendations may be adopted, modified, or rejected according to clinical needs and constraints and are not intended to replace local institutional policies. In addition, practice guidelines are not intended as standards or absolute requirements, and their use cannot guarantee any specific outcome. Practice guidelines are subject to revision as warranted by the evolution of medical knowledge, technology, and practice. They provide basic recommendations that are supported by a synthesis and analysis of the current literature, expert opinion, open forum commentary, and clinical feasibility data.

This update includes data published since the Practice Guidelines for Obstetrical Anesthesia were adopted by the American Society of Anesthesiologists in 1998; it also includes data and recommendations for a wider range of techniques than was previously addressed.

Source: "Practice Guidelines for Obstetric Anesthesia." *Anesthesiology*. 2007;106:843–863. Reprinted with permission from Lippincott Williams & Wilkins.

19.1 Methodology

19.1.1 A. Definition of Perioperative Obstetric Anesthesia

For the purposes of these Guidelines, *obstetric anesthesia* refers to peripartum anesthetic and analgesic activities performed during labor and vaginal delivery, cesarean delivery, removal of retained placenta, and postpartum tubal ligation.

19.1.2 B. Purposes of the Guidelines

The purposes of these Guidelines are to enhance the quality of anesthetic care for obstetric patients, improve patient safety by reducing the incidence and severity of anesthesia-related complications, and increase patient satisfaction.

19.1.3 C. Focus

These Guidelines focus on the anesthetic management of pregnant patients during labor, nonoperative delivery, operative delivery, and selected aspects of postpartum care and analgesia (i.e., neuraxial opioids for postpartum analgesia after neuraxial anesthesia for cesarean delivery). The intended patient population includes, but is not limited to, intrapartum and postpartum patients with uncomplicated pregnancies or with common obstetric problems. The Guidelines do not apply to patients undergoing surgery during pregnancy, gynecologic patients, or parturients with chronic medical disease (e.g., severe cardiac, renal, or neurologic disease). In addition, these Guidelines do not address (1) postpartum analgesia for vaginal delivery, (2) analgesia after tubal ligation, or (3) postoperative analgesia after general anesthesia (GA) for cesarean delivery.

19.1.4 D. Application

These Guidelines are intended for use by anesthesiologists. They also may serve as a resource for other anesthesia providers and healthcare professionals who advise or care for patients who will receive anesthetic care during labor, delivery, and the immediate postpartum period.

19.1.5 E. Task Force Members and Consultants

The American Society of Anesthesiologists (ASA) appointed a Task Force of 11 members to (1) review the published evidence, (2) obtain the opinion of a panel of consultants including anesthesiologists and nonanesthesiologist physicians concerned with obstetric anesthesia and analgesia, and (3) obtain opinions from practitioners likely to be affected by the Guidelines. The Task Force included anesthesiologists in both private and academic practices from various geographic areas of the United States and two consulting methodologists from the ASA Committee on Standards and Practice Parameters.

The Task Force developed the Guidelines by means of a seven-step process. First, they reached consensus on the criteria for evidence. Second, original published research studies from peer-reviewed journals relevant to obstetric anesthesia were reviewed. Third, the panel of expert consultants was asked to (1) participate in opinion surveys on the effectiveness of various peripartum management strategies and (2) review and comment on a draft of the Guidelines developed by the Task Force. Fourth, opinions about the Guideline recommendations were solicited from active members of the ASA who provide obstetric anesthesia. Fifth, the Task Force held open forums at two major national meetings to solicit input on its draft recommendations. Sixth, the consultants were surveyed to assess their opinions on the feasibility of implementing the Guidelines. Seventh, all available information was used to build consensus within the Task Force to finalize the Guidelines.

19.1.6 F. Availability and Strength of Evidence

Preparation of these Guidelines followed a rigorous methodologic process. To convey the findings in a concise and easy-to-understand fashion, these Guidelines use several descriptive terms. When sufficient numbers of studies are available for evaluation, the following terms describe the strength of the findings.

Support: Meta-analysis of a sufficient number of randomized controlled trials[3] indicates a statistically significant

relationship ($P < 0.01$) between a clinical intervention and a clinical outcome.

Suggest: Information from case reports and observational studies permits inference of a relationship between an intervention and an outcome. A meta-analytic assessment of this type of qualitative or descriptive information is not conducted.

Equivocal: Either a meta-analysis has not found significant differences among groups or conditions, or there is insufficient quantitative information to conduct a meta-analysis and information collected from case reports and observational studies does *not* permit inference of a relationship between an intervention and an outcome.

The *lack* of scientific evidence in the literature is described by the following terms.

Silent: No identified studies address the specified relationship between an intervention and outcome.

Insufficient: There are too few published studies to investigate a relationship between an intervention and outcome.

Inadequate: The available studies cannot be used to assess the relationship between an intervention and an outcome. These studies either do not meet the criteria for content as defined in the Focus section of these Guidelines, or do not permit a clear causal interpretation of findings due to methodologic concerns.

Formal survey information is collected from consultants and members of the ASA. The following terms describe survey responses for any specified issue. Responses are solicited on a five-point scale ranging from 1 (strongly disagree) to 5 (strongly agree), with a score of 3 being equivocal. Survey responses are summarized based on median values as follows:

Strongly Agree: Median score of 5 (at least 50% of the responses are 5)

Agree: Median score of 4 (at least 50% of the responses are 4 or 4 and 5)

Equivocal: Median score of 3 (at least 50% of the responses are 3, or no other response category or combination of similar categories contain at least 50% of the responses)

Disagree: Median score of 2 (at least 50% of the responses are 2 or 1 and 2)
Strongly Disagree: Median score of 1 (at least 50% of the responses are 1)

19.1.7 Guidelines

I. Perianesthetic Evaluation

1. History and Physical Examination. Although comparative studies are insufficient to evaluate the peripartum impact of conducting a focused history (e.g., reviewing medical records) or a physical examination, the literature reports certain patient or clinical characteristics that may be associated with obstetric complications. These characteristics include, but are not limited to, preeclampsia, pregnancy-related hypertensive disorders, HELLP syndrome, obesity, and diabetes.

The consultants and ASA members both strongly agree that a directed history and physical examination, as well as communication between anesthetic and obstetric providers, reduces maternal, fetal, and neonatal complications.

Recommendations: The anesthesiologist should conduct a focused history and physical examination before providing anesthesia care. This should include, but is not limited to, a maternal health and anesthetic history, a relevant obstetric history, a baseline blood pressure measurement, and an airway, heart, and lung examination, consistent with the ASA "Practice Advisory for Preanesthesia Evaluation."[4] When a neuraxial anesthetic is planned or placed, the patient's back should be examined.

Recognition of significant anesthetic or obstetric risk factors should encourage consultation between the obstetrician and the anesthesiologist. A communication system should be in place to encourage early and ongoing contact between obstetric providers, anesthesiologists, and other members of the multidisciplinary team.

2. Intrapartum Platelet Count. The literature is insufficient to assess whether a routine platelet count can predict anesthesia-related complications in uncomplicated parturients. The literature suggests that a platelet count is clinically useful

for parturients with suspected pregnancy-related hypertensive disorders, such as preeclampsia or HELLP syndrome, and for other disorders associated with coagulopathy.

The ASA members are equivocal, but the consultants agree that obtaining a routine intrapartum platelet count does *not* reduce maternal anesthetic complications. Both the consultants and ASA members agree that, for patients with suspected preeclampsia, a platelet count reduces maternal anesthetic complications. The consultants strongly agree and the ASA members agree that a platelet count reduces maternal anesthetic complications for patients with suspected coagulopathy.

Recommendations: A specific platelet count predictive of neuraxial anesthetic complications has not been determined. The anesthesiologist's decision to order or require a platelet count should be individualized and based on a patient's history, physical examination, and clinical signs. A routine platelet count is not necessary in the healthy parturient.

3. Blood Type and Screen. The literature is insufficient to determine whether obtaining a blood type and screen is associated with fewer maternal anesthetic complications. In addition, the literature is insufficient to determine whether a blood cross-match is necessary for healthy and uncomplicated parturients. The consultants and ASA members agree that an intrapartum blood sample should be sent to the blood bank for all parturients.

Recommendations: A routine blood cross-match is not necessary for healthy and uncomplicated parturients for vaginal or operative delivery. The decision whether to order or require a blood type and screen, or cross-match, should be based on maternal history, anticipated hemorrhagic complications (e.g., placenta accreta in a patient with placenta previa and previous uterine surgery), and local institutional policies.

4. Perianesthetic Recording of the Fetal Heart Rate. The literature suggests that anesthetic and analgesic agents may influence the fetal heart rate pattern. There is insufficient literature to demonstrate that perianesthetic recording of the fetal heart rate prevents fetal or neonatal complications. Both the consultants and ASA members agree, however, that perianesthetic recording of the fetal heart rate reduces fetal and neonatal complications.

Recommendations: The fetal heart rate should be monitored by a qualified individual before and after administration of neuraxial analgesia for labor. The Task Force recognizes that *continuous* electronic recording of the fetal heart rate may not be necessary in every clinical setting and may not be possible during initiation of neuraxial anesthesia.

II. Aspiration Prevention

1. Clear Liquids. There is insufficient published evidence to draw conclusions about the relationship between fasting times for clear liquids and the risk of emesis/reflux or pulmonary aspiration during labor. The consultants and ASA members both agree that oral intake of clear liquids during labor improves maternal comfort and satisfaction. Although the ASA members are equivocal, the consultants agree that oral intake of clear liquids during labor *does not* increase maternal complications.

Recommendations: The oral intake of modest amounts of clear liquids may be allowed for uncomplicated laboring patients. The uncomplicated patient undergoing elective cesarean delivery may have modest amounts of clear liquids up to 2 h before induction of anesthesia. Examples of clear liquids include, but are not limited to, water, fruit juices without pulp, carbonated beverages, clear tea, black coffee, and sports drinks.[5] The volume of liquid ingested is less important than the presence of particulate matter in the liquid ingested. However, patients with additional risk factors for aspiration (e.g., morbid obesity, diabetes, difficult airway) or patients at increased risk for operative delivery (e.g., nonreassuring fetal heart rate pattern) may have further restrictions of oral intake, determined on a case-by-case basis.

2. Solids. A specific fasting time for solids that is predictive of maternal anesthetic complications has not been determined. There is insufficient published evidence to address the safety of *any* particular fasting period for solids in obstetric patients. The consultants and ASA members both agree that the oral intake of solids during labor increases maternal complications. They both strongly agree that patients undergoing either elective cesarean delivery or postpartum tubal ligation should undergo

a fasting period of 6–8 h depending on the type of food ingested (e.g., fat content).[5] The Task Force recognizes that in laboring patients the timing of delivery is uncertain; therefore, compliance with a predetermined fasting period before nonelective surgical procedures is not always possible.

Recommendations: Solid foods should be avoided in laboring patients. The patient undergoing elective surgery (e.g., scheduled cesarean delivery or postpartum tubal ligation) should undergo a fasting period for solids of 6–8 h depending on the type of food ingested (e.g., fat content).[5]

3. Antacids, H2 Receptor Antagonists, and Metoclopramide. 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. Published evidence supports the efficacy of preoperative nonparticulate antacids (e.g., sodium citrate, sodium bicarbonate) in decreasing gastric acidity during the peripartum period. However, the literature is insufficient to examine the impact of nonparticulate antacids on gastric volume. The literature suggests that H_2 receptor antagonists are effective in decreasing gastric acidity in obstetric patients and supports the efficacy of metoclopramide in reducing peripartum nausea and vomiting. The consultants and ASA members agree that the administration of a nonparticulate antacid before operative procedures reduces maternal complications.

Recommendations: Before surgical procedures (i.e., cesarean delivery, postpartum tubal ligation), practitioners should consider the timely administration of nonparticulate antacids, H_2 receptor antagonists, and/or metoclopramide for aspiration prophylaxis.

III. Anesthetic Care for Labor and Vaginal Delivery

1. Overview. Not all women require anesthetic care during labor or delivery. For women who request pain relief for labor and/or delivery, there are many effective analgesic techniques available. Maternal request represents sufficient justification for pain relief. In addition, maternal medical and obstetric

conditions may warrant the provision of neuraxial techniques to improve maternal and neonatal outcome.

The choice of analgesic technique depends on the medical status of the patient, progress of labor, and resources at the facility. When sufficient resources (e.g., anesthesia and nursing staff) are available, neuraxial catheter techniques should be one of the analgesic options offered. The choice of a specific neuraxial block should be individualized and based on anesthetic risk factors, obstetric risk factors, patient preferences, progress of labor, and resources at the facility.

When neuraxial catheter techniques are used for analgesia during labor or vaginal delivery, the primary goal is to provide adequate maternal analgesia with minimal motor block (e.g., achieved with the administration of local anesthetics at low concentrations with or without opioids).

When a neuraxial technique is chosen, appropriate resources for the treatment of complications (e.g., hypotension, systemic toxicity, high spinal anesthesia) should be available. If an opioid is added, treatments for related complications (e.g., pruritus, nausea, respiratory depression) should be available. An intravenous infusion should be established before the initiation of neuraxial analgesia or anesthesia and maintained throughout the duration of the neuraxial analgesic or anesthetic. However, administration of a fixed volume of intravenous fluid is not required before neuraxial analgesia is initiated.

2. Timing of Neuraxial Analgesia and Outcome of Labor. Meta-analysis of the literature determined that the timing of neuraxial analgesia does not affect the frequency of cesarean delivery. The literature also suggests that other delivery outcomes (i.e., spontaneous or instrumented) are also unaffected. The consultants strongly agree and the ASA members agree that early initiation of epidural analgesia (i.e., at cervical dilations of less than 5 cm vs. equal to or greater than 5 cm) improves analgesia. They both *disagree* that motor block or maternal, fetal, or neonatal side effects are increased by early administration.

Recommendations: Patients in early labor (i.e., 5 cm dilation) should be given the option of neuraxial analgesia when this service is available. Neuraxial analgesia should not be withheld

on the basis of achieving an arbitrary cervical dilation, and should be offered on an individualized basis. Patients may be reassured that the use of neuraxial analgesia does not increase the incidence of cesarean delivery.

3. Neuraxial Analgesia and Trial of Labor after Previous Cesarean Delivery. Nonrandomized comparative studies suggest that epidural analgesia may be used in a trial of labor for previous cesarean delivery patients without adversely affecting the incidence of vaginal delivery. Randomized comparisons of epidural vs. other anesthetic techniques were not found. The consultants and ASA members agree that neuraxial techniques improve the likelihood of vaginal delivery for patients attempting vaginal birth after cesarean delivery.

Recommendations: Neuraxial techniques should be offered to patients attempting vaginal birth after previous cesarean delivery. For these patients, it is also appropriate to consider early placement of a neuraxial catheter that can be used later for labor analgesia, or for anesthesia in the event of operative delivery.

4. Early Insertion of a Spinal or Epidural Catheter for Complicated Parturients. The literature is insufficient to assess whether, when caring for the complicated parturient, the early insertion of a spinal or epidural catheter, with later administration of analgesia, improves maternal or neonatal outcomes. The consultants and ASA members agree that early insertion of a spinal or epidural catheter for complicated parturients reduces maternal complications.

Recommendations: Early insertion of a spinal or epidural catheter for obstetric (e.g., twin gestation or preeclampsia) or anesthetic indications (e.g., anticipated difficult airway or obesity) should be considered to reduce the need for GA if an emergent procedure becomes necessary. In these cases, the insertion of a spinal or epidural catheter may precede the onset of labor or a patient's request for labor analgesia.

5. Continuous Infusion Epidural Analgesia. *CIE Compared with Parenteral Opioids.* The literature suggests that the use of continuous infusion epidural (CIE) local anesthetics with or without opioids provides greater quality of analgesia compared with parenteral (i.e., intravenous or intramuscular) opioids. The consultants and ASA members strongly agree that CIE local

anesthetics with or without opioids provide improved analgesia compared with parenteral opioids. Meta-analysis of the literature indicates that there is a longer duration of labor, with an average duration of 24 min for the second stage, and a lower frequency of spontaneous vaginal delivery when continuous epidural local anesthetics are administered compared with *intravenous* opioids.

Meta-analysis of the literature determined that there are no differences in the frequency of cesarean delivery. Neither the consultants nor ASA members agree that CIE local anesthetics compared with parenteral opioids significantly (1) increase the duration of labor, (2) decrease the chance of spontaneous delivery, (3) increase maternal side effects, or (4) increase fetal and neonatal side effects.

6. CIE Compared with Single-injection Spinal. There is insufficient literature to assess the analgesic efficacy of CIE local anesthetics with or without opioids compared to *single-injection spinal opioids* with or without local anesthetics. The consultants are equivocal, but the ASA members agree that CIE local anesthetics improve analgesia compared with single-injection spinal opioids; both the consultants and ASA members are equivocal regarding the frequency of motor block. The consultants are equivocal, but the ASA members disagree that the use of CIE compared with single-injection spinal opioids increases the duration of labor. They both *disagree* that CIE local anesthetics with or without opioids compared to single-injection spinal opioids with or without local anesthetics decreases the likelihood of spontaneous delivery or increases maternal, fetal, or neonatal side effects.

7. CIE with and without Opioids. The literature supports the *induction* of analgesia using epidural local anesthetics combined *with opioids* compared with equal concentrations of epidural local anesthetics *without opioids* for improved quality and longer duration of analgesia. The consultants strongly agree and the ASA members agree that the addition of opioids to epidural local anesthetics improves analgesia; they both disagree that fetal or neonatal side effects are increased. The consultants disagree, but the ASA members are equivocal regarding whether the addition of opioids increases maternal side effects.

The literature is insufficient to determine whether induction of analgesia using local anesthetics with opioids compared with *higher concentrations* of epidural local anesthetics without opioids provides improved quality or duration of analgesia. The consultants and ASA members are equivocal regarding improved analgesia, and they both disagree that maternal, fetal, or neonatal side effects are increased using lower concentrations of epidural local anesthetics with opioids.

For *maintenance of analgesia*, the literature suggests that there are no differences in the analgesic efficacy of *low concentrations* of epidural local anesthetics with opioids compared with *higher concentrations* of epidural local anesthetics without opioids. The Task Force notes that the addition of an opioid to a local anesthetic infusion allows an even lower concentration of local anesthetic for providing equally effective analgesia. However, the literature is insufficient to examine whether a bupivacaine infusion concentration of *less than or equal to 0.125%* with an opioid provides comparable or improved analgesia compared with a bupivacaine concentration *greater than* 0.125% without an opioid[6]. Meta-analysis of the literature determined that low concentrations of epidural local anesthetics with opioids compared with higher concentrations of epidural local anesthetics without opioids are associated with reduced motor block. No differences in the duration of labor, mode of delivery, or neonatal outcomes are found when epidural local anesthetics with opioids are compared with epidural local anesthetics without opioids. The literature is insufficient to determine the effects of epidural local anesthetics with opioids on other maternal outcomes (e.g., hypotension, nausea, pruritus, respiratory depression, urinary retention).

The consultants and ASA members both agree that maintenance of epidural analgesia using *low* concentrations of local anesthetics with opioids provides improved analgesia compared with *higher* concentrations of local anesthetics without opioids. The consultants agree, but the ASA members are equivocal regarding the improved likelihood of spontaneous delivery when lower concentrations of local anesthetics with opioids are used. The consultants strongly agree and the ASA members agree that motor block is reduced. They agree that

maternal side effects are reduced with this drug combination. They are both equivocal regarding a reduction in fetal and neonatal side effects.

Recommendations: The selected analgesic/anesthetic technique should reflect patient needs and preferences, practitioner preferences or skills, and available resources. The continuous epidural infusion technique may be used for effective analgesia for labor and delivery. When a continuous epidural infusion of local anesthetic is selected, an opioid may be added to reduce the concentration of local anesthetic, improve the quality of analgesia, and minimize motor block.

Adequate analgesia for uncomplicated labor and delivery should be administered with the secondary goal of producing as little motor block as possible by using dilute concentrations of local anesthetics with opioids. The lowest concentration of local anesthetic infusion that provides adequate maternal analgesia and satisfaction should be administered. For example, an infusion concentration greater than 0.125% bupivacaine is unnecessary for labor analgesia in most patients.

8. Single-injection Spinal Opioids with or without Local Anesthetics. The literature suggests that spinal opioids with or without local anesthetics provide effective analgesia during labor without altering the incidence of neonatal complications. There is insufficient literature to compare spinal opioids with parenteral opioids. There is also insufficient literature to compare single-injection spinal opioids *with* local anesthetics vs. single-injection spinal opioids *without* local anesthetics.

The consultants strongly agree and the ASA members agree that spinal opioids provide improved analgesia compared with parenteral opioids. They both disagree that, compared with parenteral opioids, spinal opioids increase the duration of labor, decrease the chance of spontaneous delivery, or increase fetal and neonatal side effects. The consultants are equivocal, but the ASA members disagree that maternal side effects are increased with spinal opioids.

Compared with spinal opioids *without* local anesthetics, the consultants and ASA members both agree that spinal opioids *with* local anesthetics provide improved analgesia. They both disagree that the chance of spontaneous delivery is decreased and that fetal and neonatal side effects are increased. They are

both equivocal regarding an increase in maternal side effects. However, they both agree that motor block is increased when local anesthetics are added to spinal opioids. Finally, the consultants disagree, but the ASA members are equivocal regarding an increase in the duration of labor.

Recommendations: Single-injection spinal opioids with or without local anesthetics may be used to provide effective, although time-limited, analgesia for labor when spontaneous vaginal delivery is anticipated. If labor is expected to last longer than the analgesic effects of the spinal drugs chosen or if there is a good possibility of operative delivery, a catheter technique instead of a single-injection technique should be considered. A local anesthetic may be added to a spinal opioid to increase duration and improve quality of analgesia. The Task Force notes that the rapid onset of analgesia provided by single-injection spinal techniques may be advantageous for selected patients (e.g., those in advanced labor).

9. Pencil-point Spinal Needles. The literature supports the use of pencil-point spinal needles compared with cutting-bevel spinal needles to reduce the frequency of post-dural puncture headache. The consultants and ASA members both strongly agree that the use of pencil-point spinal needles reduces maternal complications.

Recommendations: Pencil-point spinal needles should be used instead of cutting-bevel spinal needles to minimize the risk of post-dural puncture headache.

10. Combined Spinal-Epidural Analgesia. The literature supports a faster onset time and equivalent analgesia with combined spinal-epidural (CSE) local anesthetics with opioids vs. epidural local anesthetics with opioids. The literature is equivocal regarding the impact of CSE vs. epidural local anesthetics with opioids on maternal satisfaction with analgesia, mode of delivery, hypotension, motor block, nausea, fetal heart rate changes, and Apgar scores. Meta-analysis of the literature indicates that the frequency of pruritus is increased with CSE. The consultants and ASA members both agree that CSE local anesthetics with opioids provide improved early analgesia compared with epidural local anesthetics with opioids. They are equivocal regarding the impact of CSE with opioids on overall analgesic efficacy, duration of labor, and motor block.

The consultants and ASA members both disagree that CSE increases the risk of fetal or neonatal side effects. The consultants disagree, but the ASA members are equivocal regarding whether CSE increases the incidence of maternal side effects.

Recommendations: Combined spinal-epidural techniques may be used to provide effective and rapid onset of analgesia for labor.

11. Patient-controlled Epidural Analgesia. The literature supports the efficacy of patient-controlled epidural analgesia (PCEA) vs. CIE in providing equivalent analgesia with reduced drug consumption. Meta-analysis of the literature indicates that the duration of labor is longer with PCEA compared with CIE for the first stage (e.g., an average of 36 min) but not the second stage of labor. Meta-analysis of the literature also determined that mode of delivery, frequency of motor block, and Apgar scores are equivalent when PCEA administration is compared with CIE. The literature supports greater analgesic efficacy for PCEA with a background infusion compared with PCEA without a background infusion; meta-analysis of the literature also indicates no differences in the mode of delivery or frequency of motor block. The consultants and ASA members agree that PCEA compared with CIE improves analgesia and reduces the need for anesthetic interventions; they also agree that PCEA improves maternal satisfaction. The consultants and ASA members are equivocal regarding a reduction in motor block, an increased likelihood of spontaneous delivery, or a decrease in maternal side effects with PCEA compared with CIE. They both agree that PCEA with a background infusion improves analgesia, improves maternal satisfaction, and reduces the need for anesthetic intervention. The ASA members are equivocal, but the consultants disagree that a background infusion decreases the chance of spontaneous delivery or increases maternal side effects. The consultants and ASA members are equivocal regarding the effect of a background infusion on the incidence of motor block.

Recommendations: Patient-controlled epidural analgesia may be used to provide an effective and flexible approach for the maintenance of labor analgesia. The Task Force notes that the use of PCEA may be preferable to fixed-rate CIE for providing fewer anesthetic interventions and reduced dosages

of local anesthetics. PCEA may be used with or without a background infusion.

IV. Removal of Retained Placenta

1. Anesthetic Techniques. The literature is insufficient to assess whether a particular type of anesthetic is more effective than another for removal of retained placenta. The consultants strongly agree and the ASA members agree that, if a functioning epidural catheter is in place and the patient is hemodynamically stable, epidural anesthesia is the preferred technique for the removal of retained placenta. The consultants and ASA members both agree that, in cases involving major maternal hemorrhage, GA is preferred over neuraxial anesthesia.

Recommendations: The Task Force notes that, in general, there is no preferred anesthetic technique for removal of retained placenta. However, if an epidural catheter is in place and the patient is hemodynamically stable, epidural anesthesia is preferable. Hemodynamic status should be assessed before administering neuraxial anesthesia. Aspiration prophylaxis should be considered. Sedation/analgesia should be titrated carefully due to the potential risks of respiratory depression and pulmonary aspiration during the immediate postpartum period. In cases involving major maternal hemorrhage, GA with an endotracheal tube may be preferable to neuraxial anesthesia.

2. Uterine Relaxation. The literature suggests that nitroglycerin is effective for uterine relaxation during the removal of retained placenta. The consultants and ASA members both agree that the administration of nitroglycerin for uterine relaxation improves success in removing a retained placenta.

Recommendations: Nitroglycerin may be used as an alternative to terbutaline sulfate or general endotracheal anesthesia with halogenated agents for uterine relaxation during removal of retained placental tissue. Initiating treatment with incremental doses of intravenous or sublingual (i.e., metered dose spray) nitroglycerin may relax the uterus sufficiently while minimizing potential complications (e.g., hypotension).

V. Anesthetic Choices for Cesarean Delivery

1. Equipment, Facilities, and Support Personnel. The literature is insufficient to evaluate the benefit of providing equipment, facilities and support personnel in the labor and delivery operating suite comparable to that available in the main operating suite. The consultants and ASA members strongly agree that the available equipment, facilities, and support personnel should be comparable.

Recommendations: Equipment, facilities, and support personnel available in the labor and delivery operating suite should be comparable to those available in the main operating suite. Resources for the treatment of potential complications (e.g., failed intubation, inadequate analgesia, hypotension, respiratory depression, pruritus, vomiting) should also be available in the labor and delivery operating suite. Appropriate equipment and personnel should be available to care for obstetric patients recovering from major neuraxial anesthesia or GA.

2. General, Epidural, Spinal, or Combined Spinal–Epidural Anesthesia. The literature suggests that induction-to-delivery times for GA are lower compared with epidural or spinal anesthesia and that a higher frequency of maternal hypotension may be associated with epidural or spinal techniques. Meta-analysis of the literature found that Apgar scores at 1 and 5 min are lower for GA compared with epidural anesthesia and suggests that Apgar scores are lower for GA vs. spinal anesthesia. The literature is equivocal regarding differences in umbilical artery pH values when GA is compared with epidural or spinal anesthesia.

The consultants and ASA members agree that GA reduces the time to skin incision when compared with either epidural or spinal anesthesia; they also agree that GA increases maternal complications. The consultants are equivocal and the ASA members agree that GA increases fetal and neonatal complications. The consultants and ASA members both agree that epidural anesthesia increases the time to skin incision and decreases the quality of anesthesia compared with spinal anesthesia. They both disagree that epidural anesthesia increases maternal complications.

When spinal anesthesia is compared with epidural anesthesia, meta-analysis of the literature found that induction-to-delivery times are shorter for spinal anesthesia. The literature is equivocal regarding hypotension, umbilical pH values, and Apgar scores. The consultants and ASA members agree that epidural anesthesia increases time to skin incision and reduces the quality of anesthesia when compared with spinal anesthesia. They both disagree that epidural anesthesia increases maternal complications.

When CSE is compared with epidural anesthesia, metaanalysis of the literature found no differences in the frequency of hypotension or in 1-min Apgar scores; the literature is insufficient to evaluate outcomes associated with the use of CSE compared with spinal anesthesia. The consultants and ASA members agree that CSE anesthesia improves anesthesia and reduces time to skin incision when compared with *epidural* anesthesia. The ASA members are equivocal, but the consultants disagree that maternal side effects are reduced. The consultants and ASA members both disagree that CSE improves anesthesia compared with *spinal* anesthesia. The ASA members are equivocal, but the consultants disagree that maternal side effects are reduced. The consultants strongly agree and the ASA members agree that CSE compared with spinal anesthesia increases flexibility of prolonged procedures, and they both agree that the time to skin incision is increased.

Recommendations: The decision to use a particular anesthetic technique for cesarean delivery should be individualized, based on several factors. These include anesthetic, obstetric, or fetal risk factors (e.g., elective vs. emergency), the preferences of the patient, and the judgment of the anesthesiologist. Neuraxial techniques are preferred to GA for most cesarean deliveries. An indwelling epidural catheter may provide equivalent onset of anesthesia compared with initiation of spinal anesthesia for urgent cesarean delivery. If spinal anesthesia is chosen, pencil-point spinal needles should be used instead of cutting-bevel spinal needles. However, GA may be the most appropriate choice in some circumstances (e.g., profound fetal bradycardia, ruptured uterus, severe hemorrhage, severe placental abruption). Uterine displacement (usually left

displacement) should be maintained until delivery regardless of the anesthetic technique used.

3. Intravenous Fluid Preloading. The literature supports and the consultants and ASA members agree that intravenous fluid preloading for spinal anesthesia reduces the frequency of maternal hypotension when compared with no fluid preloading.

Recommendations: Intravenous fluid preloading may be used to reduce the frequency of maternal hypotension after spinal anesthesia for cesarean delivery. Although fluid preloading reduces the frequency of maternal hypotension, initiation of spinal anesthesia should not be delayed to administer a fixed volume of intravenous fluid.

4. Ephedrine or Phenylephrine. The literature supports the administration of ephedrine and 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. The consultants agree and the ASA members strongly agree that ephedrine is acceptable for treating hypotension during neuraxial anesthesia. The consultants strongly agree and the ASA members agree that phenylephrine is an acceptable agent for the treatment of hypotension.

Recommendations: Intravenous ephedrine and phenylephrine are both acceptable drugs for treating hypotension during neuraxial anesthesia. In the absence of maternal bradycardia, phenylephrine may be preferable because of improved fetal acid–base status in uncomplicated pregnancies.

5. Neuraxial Opioids for Postoperative Analgesia. 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. The consultants strongly agree and the ASA members agree that neuraxial opioids for postoperative analgesia improve analgesia and maternal satisfaction.

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

VI. Postpartum Tubal Ligation

There is insufficient literature to evaluate the benefits of neuraxial anesthesia compared with GA for postpartum tubal ligation. In addition, the literature is insufficient to evaluate the impact of the timing of a postpartum tubal ligation on maternal outcome. The consultants and ASA members both agree that neuraxial anesthesia for postpartum tubal ligation reduces complications compared with GA. The ASA members are equivocal but the consultants agree that a postpartum tubal ligation within 8 h of delivery *does not* increase maternal complications.

Recommendations: For postpartum tubal ligation, the patient should have no oral intake of solid foods within 6–8 h of the surgery, depending on the type of food ingested (e.g., fat content). Aspiration prophylaxis should be considered. Both the timing of the procedure and the decision to use a particular anesthetic technique (i.e., neuraxial vs. general) should be individualized, based on anesthetic risk factors, obstetric risk factors (e.g., blood loss), and patient preferences. However, neuraxial techniques are preferred to GA for most postpartum tubal ligations. The anesthesiologist should be aware that gastric emptying will be delayed in patients who have received opioids during labor, and that an epidural catheter placed for labor may be more likely to fail with longer postdelivery time intervals. If a postpartum tubal ligation is to be performed before the patient is discharged from the hospital, the procedure should not be attempted at a time when it might compromise other aspects of patient care on the labor and delivery unit.

VII. Management of Obstetric and Anesthetic Emergencies

1. Resources for Management of Hemorrhagic Emergencies. Observational studies and case reports suggest that the availability of resources for hemorrhagic emergencies may be associated with reduced maternal complications. The consultants and ASA members both strongly agree that the availability of resources for managing hemorrhagic emergencies reduces maternal complications.

Recommendations: Institutions providing obstetric care should have resources available to manage hemorrhagic emergencies (Table B-1). In an emergency, the use of type-specific or O-negative blood is acceptable. In cases of intractable hemorrhage when banked blood is not available or the patient refuses banked blood, intraoperative cell-salvage should be considered if available.

Table B–1. Suggested Resources for Obstetric Hemorrhagic Emergencies

- Large-bore intravenous catheters
- Fluid warmer
- Forced-air body warmer
- Availability of blood bank resources
- Equipment for infusing intravenous fluids and blood products rapidly. Examples include, but are not limited to, hand-squeezed fluid chambers, hand-inflated pressure bags, and automatic infusion devices

The items listed represent suggestions. The items should be customized to meet the specific needs, preferences, and skills of the practitioner and health-care facility.

2. Central Invasive Hemodynamic Monitoring. There is insufficient literature to examine whether pulmonary artery catheterization is associated with improved maternal, fetal, or neonatal outcomes in patients with pregnancy-related hypertensive disorders. The literature is silent regarding the management of obstetric patients with central venous catheterization alone. The consultants and ASA members agree that the routine use

of central venous or pulmonary artery catheterization does not reduce maternal complications in severely preeclamptic patients.

Recommendations: 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. The Task Force recognizes that not all practitioners have access to resources for use of central venous or pulmonary artery catheters in obstetric units.

3. Equipment for Management of Airway Emergencies. Case reports suggest that the availability of equipment for the management of airway emergencies may be associated with reduced maternal, fetal, and neonatal complications. The consultants and ASA members both strongly agree that the immediate availability of equipment for the management of airway emergencies reduces maternal, fetal, and neonatal complications.

Recommendations: Labor and delivery units should have personnel and equipment readily available to manage airway emergencies, to include a pulse oximeter and qualitative carbon dioxide detector, consistent with the ASA Practice Guidelines for Management of the Difficult Airway[7]. Basic airway management equipment should be immediately available during the provision of neuraxial analgesia (Table B-2).

Table B–2. Suggested Resources for Airway Management during Initial Provision of Neuraxial Anesthesia

- Laryngoscope and assorted blades
- Endotracheal tubes, with stylets
- Oxygen source
- Suction source with tubing and catheters
- Self-inflating bag and mask for positive-pressure ventilation
- Medications for blood pressure support, muscle relaxation, and hypnosis
- Qualitative carbon dioxide detector
- Pulse oximeter

The items listed represent suggestions. The items should be customized to meet the specific needs, preferences, and skills of the practitioner and healthcare facility.

Table B–3. Suggested Contents of a Portable Storage Unit for Difficult Airway Management for Cesarean Delivery Rooms

Rigid laryngoscope blades of alternate design and size from those routinely used
- Laryngeal mask airway
- Endotracheal tubes of assorted size
- Endotracheal tube guides. Examples include, but are not limited to, semirigid stylets with or without a hollow core for jet ventilation, light wands, and forceps designed to manipulate the distal portion of the endotracheal tube
- Retrograde intubation equipment
- At least one device suitable for emergency nonsurgical airway ventilation. Examples include, but are not limited to, a hollow jet ventilation stylet with a transtracheal jet ventilator, and a supraglottic airway device (e.g., Combitube®, Intubating LMA [*Fastrach*™])
- Fiberoptic intubation equipment
- Equipment suitable for emergency surgical airway access (e.g., cricothyrotomy)
- An exhaled carbon dioxide detector
- Topical anesthetics and vasoconstrictors

The items listed represent suggestions. The items should be customized to meet the specific needs, preferences, and skills of the practitioner and healthcare facility.
Adapted from Practice guidelines for management of the difficult airway: An updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology.* 2003;98:1269–1277.

In addition, portable equipment for difficult airway management should be readily available in the operative area of labor and delivery units (Table B-3). The anesthesiologist should have a preformulated strategy for intubation of the difficult airway. When tracheal intubation has failed, ventilation with mask and cricoid pressure, or with a laryngeal mask airway or supraglottic airway device (e.g., Combitube®, Intubating LMA [*Fastrach*™]) should be considered for maintaining an airway and ventilating the lungs. If it is not possible to ventilate or awaken the patient, an airway should be created surgically.

4. Cardiopulmonary Resuscitation. The literature is insufficient to evaluate the efficacy of cardiopulmonary resuscitation

in the obstetric patient during labor and delivery. In cases of cardiac arrest, the American Heart Association has stated that 4–5 min is the maximum time rescuers will have to determine whether the arrest can be reversed by Basic Life Support and Advanced Cardiac Life Support interventions.[8] Delivery of the fetus may improve cardiopulmonary resuscitation of the mother by relieving aortocaval compression. The American Heart Association further notes that "the best survival rate for infants 24–25 weeks in gestation occurs when the delivery of the infant occurs no more than 5 min after the mother's heart stops beating. This typically requires that the provider begin the hysterotomy about 4 min after cardiac arrest."[8] The consultants and ASA members both strongly agree that the immediate availability of basic and advanced life-support equipment in the labor and delivery suite reduces maternal, fetal, and neonatal complications.

Recommendations: Basic and advanced life-support equipment should be immediately available in the operative area of labor and delivery units. If cardiac arrest occurs during labor and delivery, standard resuscitative measures should be initiated. In addition, uterine displacement (usually left displacement) should be maintained. If maternal circulation is not restored within 4 min, cesarean delivery should be performed by the obstetrics team.

VIII. Perianesthetic Evaluation

- Conduct a focused history and physical examination before providing anesthesia care
  - Maternal health and anesthetic history
  - Relevant obstetric history
  - Airway and heart and lung examination
  - Baseline blood pressure measurement
  - Back examination when neuraxial anesthesia is planned or placed
- A communication system should be in place to encourage early and ongoing contact between obstetric providers, anesthesiologists, and other members of the multidisciplinary team

- Order or require a platelet count based on a patient's history, physical examination, and clinical signs; a routine intrapartum platelet count is not necessary in the healthy parturient
- Order or require an intrapartum blood type and screen or crossmatch based on maternal history, anticipated hemorrhagic complications (e.g., placenta accreta in a patient with placenta previa and previous uterine surgery), and local institutional policies; a routine blood cross-match is not necessary for *healthy and uncomplicated* parturients
- The fetal heart rate should be monitored by a qualified individual before and after administration of neuraxial analgesia for labor; *continuous* electronic recording of the fetal heart rate may not be necessary in every clinical setting and may not be possible during initiation of neuraxial anesthesia

IX. Aspiration Prophylaxis

- Oral intake of modest amounts of clear liquids may be allowed for uncomplicated laboring patients
- The uncomplicated patient undergoing elective cesarean delivery may have modest amounts of clear liquids up to 2 h before induction of anesthesia
- The volume of liquid ingested is less important than the presence of particulate matter in the liquid ingested
- Patients with additional risk factors for aspiration (e.g., morbid obesity, diabetes, difficult airway) or patients at increased risk for operative delivery (e.g., nonreassuring fetal heart rate pattern) may have further restrictions of oral intake, determined on a case-by-case basis
- Solid foods should be avoided in laboring patients
- Patients undergoing elective surgery (e.g., scheduled cesarean delivery or postpartum tubal ligation) should undergo a fasting period for solids of 6–8 h depending on the type of food ingested (e.g., fat content)
- Before surgical procedures (i.e., cesarean delivery, postpartum tubal ligation), practitioners should consider timely

administration of nonparticulate antacids, H_2 receptor antagonists, and/or metoclopramide for aspiration prophylaxis

X. Anesthetic Care for Labor and Delivery

Neuraxial Techniques: Availability of Resources.

- When neuraxial techniques that include local anesthetics are chosen, appropriate resources for the treatment of complications (e.g., hypotension, systemic toxicity, high spinal anesthesia) should be available
- If an opioid is added, treatments for related complications (e.g., pruritus, nausea, respiratory depression) should be available
- An intravenous infusion should be established before the initiation of neuraxial analgesia or anesthesia and maintained throughout the duration of the neuraxial analgesic or anesthetic
- Administration of a fixed volume of intravenous fluid is not required before neuraxial analgesia is initiated

Timing of Neuraxial Analgesia and Outcome of Labor.

- Neuraxial analgesia should not be withheld on the basis of achieving an arbitrary cervical dilation, and should be offered on an individualized basis when this service is available
- Patients may be reassured that the use of neuraxial analgesia does not increase the incidence of cesarean delivery

Neuraxial Analgesia and Trial of Labor after Previous Cesarean Delivery.

- Neuraxial techniques should be offered to patients attempting vaginal birth after previous cesarean delivery
- For these patients, it is also appropriate to consider early placement of a neuraxial catheter that can be used later for labor analgesia or for anesthesia in the event of operative delivery.

Early Insertion of Spinal or Epidural Catheter for Complicated Parturients.

- Early insertion of a spinal or epidural catheter for obstetric (e.g., twin gestation or preeclampsia) or anesthetic indications (e.g., anticipated difficult airway or obesity)

should be considered to reduce the need for general anesthesia if an emergent procedure becomes necessary
  - In these cases, the insertion of a spinal or epidural catheter may precede the onset of labor or a patient's request for labor analgesia

Continuous Infusion Epidural (CIE) Analgesia.

- The selected analgesic/anesthetic technique should reflect patient needs and preferences, practitioner preferences or skills, and available resources
- CIE may be used for effective analgesia for labor and delivery
- When a continuous epidural infusion of local anesthetic is selected, an opioid may be added to reduce the concentration of local anesthetic, improve the quality of analgesia, and minimize motor block
- Adequate analgesia for uncomplicated labor and delivery should be administered with the secondary goal of producing as little motor block as possible by using dilute concentrations of local anesthetics with opioids
- The lowest concentration of local anesthetic infusion that provides adequate maternal analgesia and satisfaction should be administered

Single-injection Spinal Opioids with or without Local Anesthetics.

- Single-injection spinal opioids with or without local anesthetics may be used to provide effective, although time-limited, analgesia for labor when spontaneous vaginal delivery is anticipated
- If labor is expected to last longer than the analgesic effects of the spinal drugs chosen or if there is a good possibility of operative delivery, a catheter technique instead of a single-injection technique should be considered
- A local anesthetic may be added to a spinal opioid to increase duration and improve quality of analgesia

Pencil-point Spinal Needles.

- Pencil-point spinal needles should be used instead of cutting-bevel spinal needles to minimize the risk of postdural puncture headache

Combined Spinal-Epidural (CSE) Anesthetics.

CSE techniques may be used to provide effective and rapid analgesia for labor

Patient-controlled Epidural Analgesia (PCEA).

- PCEA may be used to provide an effective and flexible approach for the maintenance of labor analgesia
- PCEA may be preferable to CIE for providing fewer anesthetic interventions, reduced dosages of local anesthetics, and less motor blockade than fixed-rate continuous epidural infusions
- PCEA may be used with or without a background infusion

XI. Removal of Retained Placenta

- In general, there is no preferred anesthetic technique for removal of retained placenta
  - If an epidural catheter is in place and the patient is hemodynamically stable, epidural anesthesia is preferable
- Hemodynamic status should be assessed before administering neuraxial anesthesia
- Aspiration prophylaxis should be considered
- Sedation/analgesia should be titrated carefully due to the potential risks of respiratory depression and pulmonary aspiration during the immediate postpartum period
- In cases involving major maternal hemorrhage, general anesthesia with an endotracheal tube may be preferable to neuraxial anesthesia
- Nitroglycerin may be used as an alternative to terbutaline sulfate or general endotracheal anesthesia with halogenated agents for uterine relaxation during removal of retained placental tissue
  - Initiating treatment with incremental doses of intravenous or sublingual (i.e., metered dose spray) nitroglycerin may relax the uterus sufficiently while minimizing potential complications (e.g., hypotension)

XII. Anesthetic Choices for Cesarean Delivery

- Equipment, facilities, and support personnel available in the labor and delivery operating suite should be comparable to those available in the main operating suite

  - Resources for the treatment of potential complications (e.g., failed intubation, inadequate analgesia, hypotension, respiratory depression, pruritus, vomiting) should be available in the labor and delivery operating suite
  - Appropriate equipment and personnel should be available to care for obstetric patients recovering from major neuraxial or general anesthesia
- The decision to use a particular anesthetic technique should be individualized based on anesthetic, obstetric, or fetal risk factors (e.g., elective vs. emergency), the preferences of the patient, and the judgment of the anesthesiologist
  - Neuraxial techniques are preferred to general anesthesia for most cesarean deliveries
- An indwelling epidural catheter may provide equivalent onset of anesthesia compared with initiation of spinal anesthesia for urgent cesarean delivery
- If spinal anesthesia is chosen, pencil-point spinal needles should be used instead of cutting-bevel spinal needles
- General anesthesia may be the most appropriate choice in some circumstances (e.g., profound fetal bradycardia, ruptured uterus, severe hemorrhage, severe placental abruption)
- Uterine displacement (usually left displacement) should be maintained until delivery regardless of the anesthetic technique used
- Intravenous fluid preloading may be used to reduce the frequency of maternal hypotension after spinal anesthesia for cesarean delivery
- Initiation of spinal anesthesia should not be delayed to administer a fixed volume of intravenous fluid
- Intravenous ephedrine and phenylephrine are both acceptable drugs for treating hypotension during neuraxial anesthesia
  - In the absence of maternal bradycardia, phenylephrine may be preferable because of improved fetal acid–base status in uncomplicated pregnancies
- For postoperative analgesia after neuraxial anesthesia for cesarean delivery, neuraxial opioids are preferred over intermittent injections of parenteral opioids

XIII. Postpartum Tubal Ligation

- For postpartum tubal ligation, the patient should have no oral intake of solid foods within 6–8 h of the surgery, depending on the type of food ingested (e.g., fat content)
- Aspiration prophylaxis should be considered
- Both the timing of the procedure and the decision to use a particular anesthetic technique (i.e., neuraxial vs. general) should be individualized, based on anesthetic risk factors, obstetric risk factors (e.g., blood loss), and patient preferences
- Neuraxial techniques are preferred to general anesthesia for most postpartum tubal ligations
  - Be aware that gastric emptying will be delayed in patients who have received opioids during labor and that an epidural catheter placed for labor may be more likely to fail with longer postdelivery time intervals
- If a postpartum tubal ligation is to be performed before the patient is discharged from the hospital, the procedure should not be attempted at a time when it might compromise other aspects of patient care on the labor and delivery unit

XIV. Management of Obstetric and Anesthetic Emergencies

- Institutions providing obstetric care should have resources available to manage hemorrhagic emergencies
  - In an emergency, the use of type-specific or O negative blood is acceptable
  - In cases of intractable hemorrhage when banked blood is not available or the patient refuses banked blood, intraoperative cell-salvage should be considered if available
  - 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
- Labor and delivery units should have personnel and equipment readily available to manage airway emergencies, to include a pulse oximeter and qualitative carbon dioxide

detector, consistent with the ASA Practice Guidelines for Management of the Difficult Airway
  - Basic airway management equipment should be immediately available during the provision of neuraxial analgesia
  - Portable equipment for difficult airway management should be readily available in the operative area of labor and delivery units
  - The anesthesiologist should have a preformulated strategy for intubation of the difficult airway
  - When tracheal intubation has failed, ventilation with mask and cricoid pressure, or with a laryngeal mask airway or supraglottic airway device (e.g., Combitube®, Intubating LMA [*Fastrach*™]) should be considered for maintaining an airway and ventilating the lungs
  - If it is not possible to ventilate or awaken the patient, an airway should be created surgically
- Basic and advanced life-support equipment should be immediately available in the operative area of labor and delivery units
- If cardiac arrest occurs during labor and delivery, standard resuscitative measures should be initiated
  - Uterine displacement (usually left displacement) should be maintained
  - If maternal circulation is not restored within 4 min, cesarean delivery should be performed by the obstetrics team

19.2 Methods and Analyses

The scientific assessment of these Guidelines was based on evidence linkages or statements regarding potential relationships between clinical interventions and outcomes. The interventions listed below were examined to assess their impact on a variety of outcomes related to obstetric anesthesia.[9]

1. *Perianesthetic Evaluation*
   i. A directed history and physical examination
   ii. Communication between anesthetic and obstetric providers

iii. A routine intrapartum platelet count does not reduce maternal anesthetic complications
iv. For suspected preeclampsia or coagulopathy an intrapartum platelet count
v. An intrapartum blood type and screen for all parturients reduces maternal complications
vi. For healthy and uncomplicated parturients, a blood cross-match is unnecessary
vii. Perianesthetic recording of the fetal heart rate reduces fetal and neonatal complications

2. *Aspiration Prophylaxis in the Obstetric Patient*
   i. Oral intake of clear liquids during labor improves patient comfort and satisfaction but does not increase maternal complications
   ii. Oral intake of solids during labor increases maternal complications
   iii. A fasting period for solids of 6–8 h before an elective cesarean reduces maternal complications
   iv. Nonparticulate antacids vs. no antacids before operative procedures (excluding operative vaginal delivery) reduces maternal complications
3. *Anesthetic Care for Labor and Delivery*
   i. Neuraxial techniques
      a. Prophylactic spinal or epidural catheter insertion for complicated parturients reduces maternal complications
      b. Continuous epidural infusion of local anesthetics with or without opioids vs. parenteral opioids
      c. Continuous epidural infusion of local anesthetics with or without opioids vs. spinal opioids with or without local anesthetics
      d. Induction of epidural analgesia using local anesthetics with opioids vs. equal concentrations of epidural local anesthetics without opioids
      e. Induction of epidural analgesia using local anesthetics with opioids vs. higher concentrations of epidural local anesthetics without opioids
      f. Maintenance of epidural infusion of lower concentrations of local anesthetics with opioids vs.

higher concentrations of local anesthetics without opioids (e.g., bupivacaine concentrations < 0.125% with opioids vs. concentrations > 0.125% without opioids)

g. Single-injection spinal opioids with or without local anesthetics vs. parenteral opioids
h. Single-injection spinal opioids with local anesthetics vs. spinal opioids without local anesthetics

ii. Combined spinal-epidural (CSE) techniques
   a. CSE local anesthetics with opioids vs. epidural local anesthetics with opioids

iii. Patient-controlled epidural analgesia (PCEA)
   a. PCEA vs. continuous infusion epidurals
   b. PCEA with a background infusion vs. PCEA without a background infusion

iv. Neuraxial analgesia, timing of initiation, and progress of labor
   a. Administering epidural analgesia at cervical dilations of < 5 cm (vs. > 5 cm)
   b. Neuraxial techniques for patients attempting vaginal birth after previous cesarean delivery

4. *Removal of Retained Placenta*
   i. If an epidural catheter is in situ and the patient is hemodynamically stable, epidural anesthesia is preferred over general or spinal anesthesia to improve the success at removing retained placenta
   ii. In cases involving major maternal hemorrhage, general anesthesia is preferred over neuraxial anesthesia to reduce maternal complications
   iii. Administration of nitroglycerin for uterine relaxation improves success at removing retained placenta
5. *Anesthetic Choices for Cesarean Delivery*
   i. Equipment, facilities, and support personnel available in the labor and delivery suite should be comparable to that available in the main operating suite
   ii. General anesthesia vs. epidural anesthesia
   iii. General anesthesia vs. spinal anesthesia
   iv. Epidural anesthesia vs. spinal anesthesia
   v. CSE anesthesia vs. epidural anesthesia

vi. CSE anesthesia vs. spinal anesthesia
vii. Use of pencil-point spinal needles vs. cutting-bevel spinal needles reduces maternal complications
viii. Intravenous fluid preloading vs. no intravenous fluid preloading for spinal anesthesia reduces maternal hypotension
ix. Ephedrine or phenylephrine reduces maternal hypotension during neuraxial anesthesia
x. Neuraxial opioids vs. parenteral opioids for postoperative analgesia after neuraxial anesthesia for cesarean delivery

6. *Postpartum Tubal Ligation*
   i. Neuraxial anesthesia vs. general anesthesia
   ii. A postpartum tubal ligation within 8 h of delivery does not increase maternal complications
7. *Management of Complications*
   i. Availability of resources for management of hemorrhagic emergencies
   ii. Immediate availability of equipment for management of airway emergencies
   iii. Immediate availability of basic and advanced life-support equipment in the labor and delivery suite
   iv. Invasive hemodynamic monitoring for severely preeclamptic patients

Scientific evidence was derived from aggregated research literature, and opinion-based evidence was obtained from surveys, open presentations, and other activities (e.g., Internet posting). For purposes of literature aggregation, potentially relevant clinical studies were identified *via* electronic and manual searches of the literature. The electronic and manual searches covered a 67-year period from 1940 through 2006. More than 4,000 citations were initially identified, yielding a total of 2,986 nonoverlapping articles that addressed topics related to the evidence linkages. After review of the articles, 2,549 studies did not provide direct evidence and were subsequently eliminated. A total of 437 articles contained direct linkage-related evidence.

Initially, each pertinent outcome reported in a study was classified as supporting an evidence linkage, refuting a linkage, or equivocal. The results were then summarized to obtain a

directional assessment for each evidence linkage before conducting a formal meta-analysis. Literature pertaining to 11 evidence linkages contained enough studies with well-defined experimental designs and statistical information sufficient for meta-analyses. These linkages were (1) nonparticulate antacids vs. no antacids, (2) continuous epidural infusion of local anesthetics with or without opioids vs. parenteral opioids, (3) induction of epidural analgesia using local anesthetics with opioids vs. equal concentrations of epidural local anesthetics without opioids, (4) maintenance of epidural infusion of lower concentrations of local anesthetics with opioids vs. higher concentrations of local anesthetics without opioids, (5) CSE local anesthetics with opioids vs. epidural local anesthetics with opioids, (6) PCEA vs. continuous infusion epidurals, (7) general anesthesia vs. epidural anesthesia for cesarean delivery, (8) CSE anesthesia vs. epidural anesthesia for cesarean delivery, (9) use of pencil-point spinal needles vs. cutting-bevel spinal needles, (10) ephedrine or phenylephrine reduces maternal hypotension during neuraxial anesthesia, and (11) neuraxial opioids vs. parenteral opioids for postoperative analgesia after neuraxial anesthesia for cesarean delivery.

General variance-based effect-size estimates or combined probability tests were obtained for continuous outcome measures, and Mantel-Haenszel odds ratios were obtained for dichotomous outcome measures. Two combined probability tests were used as follows: (1) the Fisher combined test, producing chi-square values based on logarithmic transformations of the reported P values from the independent studies, and (2) the Stouffer combined test, providing weighted representation of the studies by weighting each of the standard normal deviates by the size of the sample. An odds ratio procedure based on the Mantel-Haenszel method for combining study results using 2×2 tables was used with outcome frequency information. An acceptable significance level was set at $P < 0.01$ (one-tailed). Tests for heterogeneity of the independent studies were conducted to assure consistency among the study results. DerSimonian-Laird random-effects odds ratios were obtained when significant heterogeneity was found ($P < 0.01$). To control for potential publishing bias, a "fail-safe n" value was calculated. No search for unpublished studies was

conducted, and no reliability tests for locating research results were done.

Meta-analytic results are reported in Table B-4 (see original report in *Anesthesiology* 2007; 106:856–857). To be accepted as significant findings, Mantel-Haenszel odds ratios must agree with combined test results whenever both types of data are assessed. In the absence of Mantel-Haenszel odds ratios, findings from both the Fisher and weighted Stouffer combined tests must agree with each other to be acceptable as significant.

Interobserver agreement among Task Force members and two methodologists was established by interrater reliability testing. Agreement levels using a k statistic for two-rater agreement pairs were as follows: (1) type of study design, $k = 0.83–0.94$; (2) type of analysis, $k = 0.71–0.93$; (3) evidence linkage assignment, $k = 0.87–1.00$; and (4) literature inclusion for database, $k = 0.74–1.00$. Three-rater chance-corrected agreement values were (1) study design, Sav = 0.884, Var (Sav) = 0.004; (2) type of analysis, Sav = 0.805, Var (Sav) = 0.009; (3) linkage assignment, Sav = 0.911, Var (Sav) = 0.002; and (4) literature database inclusion, Sav = 0.660, Var (Sav) = 0.024. These values represent moderate to high levels of agreement.

Consensus was obtained from multiple sources, including (1) survey opinion from consultants who were selected based on their knowledge or expertise in obstetric anesthesia or maternal and fetal medicine, (2) survey opinions solicited from active members of the ASA, (3) testimony from attendees of publicly held open forums at two national anesthesia meetings, (4) Internet commentary, and (5) Task Force opinion and interpretation. The survey rate of return was 75% ($n = 76$ of 102) for the consultants, and 2,326 surveys were received from active ASA members. Results of the surveys are reported in Tables B-5 and B-6 and in the text of the Guidelines (see original report in *Anesthesiology* 2007;106:858–863).

The consultants were asked to indicate which, if any, of the evidence linkages would change their clinical practices if the Guidelines were instituted. The rate of return was 35% ($n = 36$). The percent of responding consultants expecting *no change* associated with each linkage were as follows: perianesthetic evaluation – 97%; aspiration prophylaxis – 83%; anesthetic

care for labor and delivery – 89%; removal of retained placenta – 97%; anesthetic choices for cesarean delivery – 97%; postpartum tubal ligation – 97%; and management of complications – 94%. Ninety-seven percent of the respondents indicated that the Guidelines would have *no effect* on the amount of time spent on a typical case. One respondent indicated that there would be an increase of 5 min in the amount of time spent on a typical case with the implementation of these Guidelines.

19.3 References

1. Developed by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia: Joy L. Hawkins, M.D. (Chair), Denver, Colorado; James F. Arens, M.D., Houston, Texas; Brenda A Bucklin, M.D., Denver, Colorado; Richard T. Connis, Ph.D., Woodinville, Washington; Patricia A. Dailey, M.D., Hillsborough, California; David R. Gambling, M.B.B.S., San Diego, California; David G. Nickinovich, Ph.D., Bellevue, Washington; Linda S. Polley, M.D., Ann Arbor, Michigan; Lawrence C. Tsen, M.D., Boston, Massachusetts; David J. Wlody, M.D., Brooklyn, New York; and Kathryn J. Zuspan, M.D., Stillwater, Minnesota.
2. International Anesthesia Research Society, 80th Clinical and Scientific Congress,San Francisco, California, March 25, 2006; and Society of Obstetric Anesthesia and Perinatology 38th Annual Meeting, Hollywood, Florida, April 29, 2006.
3. A prospective nonrandomized controlled trial may be included in a metaanalysis under certain circumstances if specific statistical criteria are met.
4. American Society of Anesthesiologists Task Force on Preanesthesia Evaluation: Practice advisory for preanesthesia evaluation. ANESTHESIOLOGY 2002;96:485–496.
5. American Society of Anesthesiologists Task Force on Preoperative Fasting: Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration. ANESTHESIOLOGY 1999;90:896–905.
6. References to bupivacaine are included for illustrative purposes only, and because bupivacaine is the most extensively studied local anesthetic for continuous infusion epidural analgesia. The Task Force recognizes that other local anesthetics are appropriate for continuous infusion epidural analgesia.

7. American Society of Anesthesiologists Task Force on Management of the Difficult Airway: Practice guidelines for management of the difficult airway: An updated report. *Anesthesiology.* 2003;98:1269–1277.
8. 2005 American Heart Association guidelines for cardiopulmonary resuscitationand emergency cardiovascular care. Circulation 2005;112(suppl):IV1–IV203.
9. Unless otherwise specified, outcomes for the listed interventions refer to the reduction of maternal, fetal, and neonatal complications.
10. Additional outcomes include improved analgesia, analgesic use, maternal comfort, and satisfaction

Appendix C Optimal Goals for Anesthesia Care in Obstetrics

This joint statement from the American Society of Anesthesiologists (ASA) and the American College of Obstetricians and Gynecologists (ACOG) has been designed to address issues of concern to both specialties. Good obstetric care requires the availability of qualified personnel and equipment to administer general or regional anesthesia both electively and emergently. The extent and degree to which anesthesia services are available varies widely among hospitals. However, for any hospital providing obstetric care, certain optimal anesthesia goals should be sought. These include:

1. Availability of a licensed practitioner who is credentialed to administer an appropriate anesthetic whenever necessary. For many women, regional anesthesia (epidural, spinal, or combined spinal epidural) will be the most appropriate anesthetic.
2. Availability of a licensed practitioner who is credentialed to maintain support of vital functions in any obstetric emergency.
3. Availability of anesthesia and surgical personnel to permit the start of a cesarean delivery within 30 min of the decision to perform the procedure.
4. Immediate availability of appropriate facilities and personnel, including obstetric anesthesia, nursing personnel, and a physician capable of monitoring labor and performing cesarean delivery, including an emergency cesarean delivery in cases of vaginal birth after cesarean delivery

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Committee of Origin: Obstetrical Anesthesia (Approved by the ASA House of Delegates on October 17, 2007, and last amended on October 22, 2008)

(VBAC).[1] The definition of immediately available personnel and facilities remains a local decision based on each institution's available resources and geographic location.

5. Appointment of a qualified anesthesiologist to be responsible for all anesthetics administered. There are many obstetric units where obstetricians or obstetrician-supervised nurse anesthetists administer labor anesthetics. The administration of general or regional anesthesia requires both medical judgment and technical skills. Thus, a physician with privileges in anesthesiology should be readily available.

Persons administering or supervising obstetric anesthesia should be qualified to manage the infrequent but occasionally life-threatening complications of major regional anesthesia such as respiratory and cardiovascular failure, toxic local anesthetic convulsions, or vomiting and aspiration. Mastering and retaining the skills and knowledge necessary to manage these complications require adequate training and frequent application.

To ensure the safest and most effective anesthesia for obstetric patients, the Director of Anesthesia Services, with the approval of the medical staff, should develop and enforce written policies regarding provision of obstetric anesthesia. These include:

1. A qualified physician with obstetric privileges to perform operative vaginal or cesarean delivery should be readily available during administration of anesthesia. Readily available should be defined by each institution within the context of its resources and geographic location. Regional and/or general anesthesia should not be administered until the patient has been examined and the fetal status and progress of labor evaluated by a qualified individual. A physician with obstetric privileges who concurs with the patient's management and has knowledge of the maternal and fetal status and the progress of labor should be readily available to deal with any obstetric complications that may arise. A physician with obstetric privileges should be responsible for midwifery backup in hospital settings that utilize certified nurse midwives/certified midwives as obstetric providers.

2. Availability of equipment, facilities, and support personnel equal to that provided in the surgical suite. This should include the availability of a properly equipped and staffed recovery room capable of receiving and caring for all patients recovering from major regional or general anesthesia. Birthing facilities, when used for analgesia or anesthesia, must be appropriately equipped to provide safe anesthetic care during labor and delivery or postanesthesia recovery care.
3. Personnel, other than the surgical team, should be immediately available to assume responsibility for resuscitation of the depressed newborn. The surgeon and anesthesiologist are responsible for the mother and may not be able to leave her to care for the newborn, even when a regional anesthetic is functioning adequately. Individuals qualified to perform neonatal resuscitation should demonstrate:
    3.1. Proficiency in rapid and accurate evaluation of the newborn condition, including Apgar scoring.
    3.2. Knowledge of the pathogenesis of a depressed newborn (acidosis, drugs, hypovolemia, trauma, anomalies, and infection), as well as specific indications for resuscitation.
    3.3. Proficiency in newborn airway management, laryngoscopy, endotracheal intubations, suctioning of airways, artificial ventilation, cardiac massage, and maintenance of thermal stability.

In larger maternity units and those functioning as high-risk centers, 24-hour in-house anesthesia, obstetric and neonatal specialists are usually necessary. Preferably, the obstetric anesthesia services should be directed by an anesthesiologist with special training or experience in obstetric anesthesia. These units will also frequently require the availability of more sophisticated monitoring equipment and specially trained nursing personnel.

A survey jointly sponsored by ASA and ACOG found that many hospitals in the United States have not yet achieved the goals mentioned previously. Deficiencies were most evident in smaller delivery units. Some small delivery units are necessary because of geographic considerations. Currently,

approximately 34% of hospitals providing obstetric care have fewer than 500 deliveries per year.[2] Providing comprehensive care for obstetric patients in these small units is extremely inefficient, not cost-effective and frequently impossible. Thus, the following recommendations are made:

1. Whenever possible, small units should consolidate.
2. When geographic factors require the existence of smaller units, these units should be part of a well-established regional perinatal system.

The availability of the appropriate personnel to assist in the management of a variety of obstetric problems is a necessary feature of good obstetric care. The presence of a pediatrician or other trained physician at a high-risk cesarean delivery to care for the newborn or the availability of an anesthesiologist during active labor and delivery when VBAC is attempted and at a breech or multifetal delivery are examples. Frequently, these physicians spend a considerable amount of time standing by for the possibility that their services may be needed emergently, but may ultimately not be required to perform the tasks for which they are present. Reasonable compensation for these standby services is justifiable and necessary.

A variety of other mechanisms have been suggested to increase the availability and quality of anesthesia services in obstetrics. Improved hospital design, to place labor and delivery suites closer to the operating rooms, would allow for safer and more efficient anesthesia care, including supervision of nurse anesthetists. Anesthesia equipment in the labor and delivery area must be comparable to that in the operating room.

Finally, good interpersonal relations between obstetricians and anesthesiologists are important. Joint meetings between the two departments should be encouraged. Anesthesiologists should recognize the special needs and concerns of the obstetrician and obstetricians should recognize the anesthesiologist as a consultant in the management of pain and life-support measures. Both should recognize the need to provide high-quality care for all patients.

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19.1 References

1. Vaginal birth after previous cesarean delivery. ACOG Practice Bulletin No. 54. American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2004;104:203–212.
2. Bucklin BA, Hawkins JL, Anderson JR, et al. Obstetric anesthesia workforce survey: twenty-year update. *Anesthesiology*. 2005;103:645–653.

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