# 15 High-Risk Pregnancy: Pregnancy-Related Problems ▼

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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<sup>1</sup> (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<sup>78</sup> 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.<sup>2</sup> 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.<sup>3</sup>
    - 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*<sup>4</sup> *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.<sup>5</sup> (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.<sup>6,7</sup> 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.<sup>8</sup> 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.<sup>9</sup>

#### 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<sup>78</sup> with permission)

0.2–2%)<sup>1</sup> (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,

(b)			
Clinical Features	Placenta Previa	Abruptio Placentae	
Bleeding Blood	Painless Fresh	Painful Dark, old, mixed with clots	
Clotting problems Sudden fetal distress	Uncommon Uncommon	Common Common	

Table 15-1.Differential Diagnosis (Placenta Previa<br/>vs. Abruptio Placentae)

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  $\mu$ g has been used for uterine relaxation with great success.<sup>10</sup> We prefer

to use 50–100  $\mu$ g 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  $\mu$ g) 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.<sup>11</sup> 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.<sup>12</sup> 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.<sup>13</sup> 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.<sup>14–16</sup> 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.<sup>17</sup> 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:<sup>18</sup> (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.<sup>19</sup> 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.<sup>20</sup> 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.<sup>21</sup> (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<sup>80</sup> used with permission from Elsevier.)

Subjects		P <sub>50</sub> (mm Hg)	
Status	n	Mean	SEM
Nonpregnant <sup>†</sup> Pregnant	10	26.7	0.11
1st trimester <sup>†</sup>	10	27.8	0.08
2nd trimester <sup>†</sup>	10	28.8	0.17
At or near term <sup>†</sup>	24	30.4	0.20
Preeclamptic <sup>‡</sup>	14	25.1	0.38

Table 15-3. P<sub>50</sub> Values of Nonpregnant, Pregnant, and Preeclamptic Subjects

<sup>+</sup>All means are significantly different from one another (p < 0.01), Newman-Keul's test. <sup>‡</sup>Significant level of difference between pregnant at term and pre-

eclamptic at term (p < 0.001). From Kambam et al.<sup>21</sup> used with permission.

shifting of the maternal P50 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.<sup>22,23</sup> 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.<sup>24</sup> Magnesium is the accepted

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

 
 Table 15-4.
 Effects of Increasing Plasma Magnesium Levels

From Shnider and Levinson<sup>83</sup> used with permission.

specific medication for the prevention of recurrent convulsion (eclampsia).<sup>25,26</sup> 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.<sup>26</sup> 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.<sup>27</sup> Left ventricular function as . illustrated by plotting the Starling curve is shifted upwards and left.<sup>28</sup> 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.<sup>27</sup> 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.<sup>28</sup> 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.<sup>29</sup> 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.<sup>30</sup>

Benedetti et al.<sup>30,31</sup> 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<sup>2</sup>). 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<sup>32</sup> 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.<sup>32</sup>)

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).<sup>30</sup> 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.<sup>30</sup>)

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.<sup>29</sup> used with permission.)

analgesia will decrease maternal blood pressure (Fig. 15-9) and can indirectly increase placental perfusion<sup>33,34</sup> 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.<sup>35</sup> 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<sup>3</sup> 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<sup>3</sup> DeBoer and colleagues<sup>36</sup> 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) ( $\alpha^{\circ}$  [normal range = 50-60°] is the angle formed by the slope of the TEG tracing from the r to the Kvalue. 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<sup>37</sup>. 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  $\alpha$  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<sup>37</sup>. Used with permission.)

whereas Fig. 15-11 shows parturients with normal as well as abnormal bleeding conditions.<sup>37,38</sup> Orlikowski et al. studied 49 patients with preeclampsia.<sup>39</sup> 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.<sup>40</sup> They noted that patients with mild preeclampsia were hypercoaguable while patients with severe preeclampsia with platelet count less than 100,000/mm<sup>3</sup> 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<sup>3</sup> 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<sup>3</sup> after due consideration of risk benefit ratio of regional versus

general anesthesia. Sharma et al.<sup>40</sup> found that MA does not decrease until the platelet count decreases below 70,000/mm<sup>3</sup>. 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 wellconducted studies argue against this dictum.<sup>41,42</sup> 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.<sup>43</sup> As in numerous studies in normal pregnancy, preload with crystalloid (1 L Ringers lactate) did not prevent maternal hypotension in preeclamptic patients.<sup>44</sup> 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.<sup>44</sup> 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.  $50-100 \ \mu g$  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:

- Labetalol One study showed that labetalol (1 mg/kg) will decrease the maternal blood pressure without affecting the intervillous and fetal blood flow.<sup>45</sup> 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.<sup>46</sup> 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.<sup>47</sup> Recently, remifentanil has been used as an alternative in these circumstances.<sup>48,49</sup>

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. $^{50}$ 

 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.<sup>51</sup> 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

Pregnancy				
Disorder	HELLP	ТТР	HUS	Fatty Liver of Pregnancy
Microangiopathic hemolytic anemia	+	+	+	-
Thrombocytopenic bleeding	+	+	+	+
Neurological dysfunction	+	++	±	±
Renal dysfunction	±	+	+++	+

**Table 15-5.** Differential Diagnosis of HELLPSyndrome, Thrombotic Thrombocytic Purpura,Hemolytic-Uremic Syndrome, and Fatty Liver ofPregnancy

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.<sup>52'</sup> Medical records from 1997 to 2002 of parturients with platelet counts <100,000/mm<sup>3</sup> 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  $>70,000 / \text{mm}^3$ ; all received regional anesthesia for either vaginal or cesarean delivery, as did all parturients with platelet counts 70,000-60,000 / mm<sup>3</sup> 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).<sup>53</sup> 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,<sup>54,55</sup> 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.<sup>56</sup> 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
- Coagulation abnormalities (nearly universal<sup>57</sup>; 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

- 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.<sup>58</sup>

# **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:

 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.<sup>59,60</sup> Treatment of fetal fibronectin, a marker of degradation of the extracellular matrix, is often used to predict preterm delivery.<sup>61</sup>

## 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.<sup>62</sup> 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.

 $\beta$ -Adrenergic Drugs. Historically the most widely used tocolytic agents, these agents act by direct stimulation of

the  $\beta$ -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  $\beta$ -mimetic therapy, and the incidence has been reported to be 1–5% in parturients.<sup>63</sup> 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<sub>4</sub> 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  $\beta$ 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.<sup>64</sup>
- 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  $\beta$ -mimetic therapy has also been shown to increase the maternal heart rate, cardiac output, and stroke volume.<sup>65</sup>  $\beta$ -mimetic drugs can increase sodium and



**Figure 15-12.** Cardiovascular changes of  $\beta$ -sympathomimetic therapy in pregnancy. (From Hawker<sup>81</sup> used with permission.)

water retention because of increased secretion of antidiuretic hormone.<sup>64</sup> 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.<sup>66</sup>

 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  $\beta$ -mimetic therapy. (Reprinted from Benedetti,<sup>82</sup> © 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  $\mu$ g at a time, may be necessary to maintain the blood pressure. Volume expansion should be carefully regulated; O<sub>2</sub> 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<sub>4</sub> therapy can interact with both depolarizing and nondepolarizing muscle relaxants.
- 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  $\beta$ -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.<sup>67</sup>

# 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.<sup>68</sup> 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.
- 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 OxygenTension with Varying Maternal Inspired OxygenConcentration

Maternal FIO <sub>2</sub>	Maternal PaO <sub>2</sub> (mm Hg)	Umbilical Artery PaO <sub>2</sub> (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.<sup>69</sup> 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<sup>70</sup> 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<sup>71</sup> 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<sup>3</sup>.
- 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.<sup>72</sup> The former study is from evaluation of the Trauma Research Database.<sup>73</sup> 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 FEP 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.<sup>74,75</sup> 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.<sup>76,77</sup> The downside of rFVIIa use is the occurrence of strokes due to embolic phenomena and therefore this factor has to be used cautiously.<sup>77</sup> Factor VIIa is also extremely expensive. Prospective studies are currently in progress.

# Summary

There is a need for further studies on anesthetic needs for highrisk 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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