INTRODUCTION

Major scientific advances have occurred in virtually all areas of patient care. One of the major changes in obstetrics has been the recognition of the specialty nature of medical complications related to pregnancy. The physiologic alterations that accompany pregnancy may have profound effects on a variety of pathologic conditions. In addition, maternal disease or its therapy may adversely affect the fetus, which makes these considerations unique to the obstetric patient.

The intensivist must be knowledgeable of the considerations specific to pregnant women and should also understand the pathophysiologic alterations associated with high-risk conditions such as preeclampsia. Obstetricians have done a remarkably good job in managing common diseases such as diabetes, asthma, and chronic hypertension with great sophistication. Nevertheless, life-threatening emergencies during pregnancy challenge the knowledge and skills of anyone who works with this group of patients. Clinicians have acquired considerable information about the management of critically ill obstetric patients; however, this information is not geared toward the critical care provider in most textbooks. This chapter is intended to fill this gap and provide the essential information about the most severe critical conditions that might arise during pregnancy.

An extensive review of all maternal high-risk conditions would go beyond the scope of this chapter. Therefore, we will limit our review to the discussion of physiologic changes of pregnancy that clearly have to be recognized when managing the critically ill pregnant woman. This review is focused mainly on the most life-threatening pathophysiologic processes, including thrombosis and thromboembolism, hypertensive disease of pregnancy, hemorrhage, and amniotic fluid embolism (Tables 77.1 and 77.2), but is inclusive of other more common pregnancy-related problems that come to the attention of the intensivist, such as peripartum cardiomyopathy (PPCM) and pulmonary edema.

PHYSIOLOGY

Several physiologic changes are associated with normal pregnancy. These adaptations are necessary to meet the demands of the growing fetus, and have to be considered when evaluating and managing pregnant patients.

Body Constitution

Optimal weight gain in pregnancy is currently a matter of debate (1–3). In general, an approximate weight gain of 6 kg is attributed to the fetus, placenta, and uterus, with the remainder of the weight gain due to an increase in maternal blood, interstitial fluid volume, and fat. A gestational weight gain of more than 12 kg in women of normal prepregnant weight puts her into an augmented risk category—even though the lowest one—for complications during delivery. Thorsdottir et al. (4) studied the relationship between gestational weight gain and complications during pregnancy, comparing pregnant women with normal weight gain with other higher gestational weight gain. They found that women who exceeded 18 kg of weight gain during pregnancy are at greater risk for maternal (preeclampsia, gestational diabetes) and fetal (increased incidence of operative delivery) complications.

Changes in maternal physiology occur normally during pregnancy, and have the potential to alter the absorption, distribution, and elimination of drugs used therapeutically in pregnant women (5).

Metabolism and Respiration

Key physiologic changes of respiration that occur in pregnancy are an increased minute ventilation, which is caused by increased respiratory center sensitivity and drive; a compensated respiratory alkalosis; and a low expiratory reserve volume (ERV) (6,7). Vital capacity and forced expiratory measurements are well preserved. Patients who have severe lung diseases tolerate pregnancy well, with the exception of those with pulmonary hypertension or chronic respiratory insufficiency from parenchymal or neuromuscular disease.

Lung volumes have been measured in several case series, where pregnant women were compared to nonpregnant women or those in the postpartum state (8), with body plethysmography being the preferred technique of measurement (9); volumes were found to be well preserved in the majority of cases. The residual volume tends to decrease slightly, leading to no change or a small increase in the vital capacity (8,10–13). The most consistent change in static lung volumes with pregnancy is the reduction in the functional residual capacity (FRC) and ERV. As the uterus enlarges, FRC decreases by 10% to 25% of the previous value, starting about the 12th week of pregnancy (8); this decrement is accentuated further in the supine position (14). The reduction in FRC is due to a decrease in chest wall compliance of from 35% to 40% (15). The lung compliance...
remains normal during pregnancy, whereas expiratory muscle strength is in the low-normal range (10). The decreased chest wall compliance is the result of the enlarging uterus increasing abdominal pressure, leading to a reduction in FRC (16); the diaphragm elevates about 4 cm and the circumference of the lower rib cage increases about 5 cm (17). The lower end-expiratory lung volume leads to an increased area of apposition of the diaphragm to the chest wall, which improves the coupling of the diaphragm and chest wall. Thus, the increased tidal volume of pregnancy is achieved without an increase in the respiratory excursions of the diaphragm.

The rib cage undergoes structural changes during pregnancy (18). Progressive relaxation of the ligamentous attachments of the ribs causes the subcostal angle of the rib cage to increase early in pregnancy, persisting for months into the postpartum period. The increased elasticity of the rib cage is mediated by the polypeptide hormone, relaxin, which is increased during pregnancy and is responsible for the softening of the cervix and relaxation of the pelvic ligaments (19,20). Changes in pulmonary function during pregnancy are summarized in Figure 77.1.

Changes in Arterial Blood Gases

The hormonal changes of pregnancy lead to remarkable respiratory changes throughout its course. The resulting changes of arterial blood gas values have been measured by Sheldon (21) and Templeton and Kelman (22), who obtained serial measurements of maternal blood gases during pregnancy. The same investigators also measured serial alveolar-to-arterial oxygen tension differences (PAO2 – PaO2), and calculated the pulmonary venous admixture (physiologic shunt), dead space-to-tidal volume ratio (VD/VT), and respiratory minute volume (Table 77.3). The mean arterial PO2 was found to be consistently greater than 100 mmHg throughout pregnancy, with no alterations of dead space-to-tidal volume ratio (VD/VT) and shunt.

Cardiovascular System

Management of pregnancy, especially for women with heart disease, requires an understanding of gestational hemodynamic stress. The most important hemodynamic change in the maternal circulation during pregnancy is an increase in the cardiac output up to 45% (23), which can be primarily attributed to an increase in stroke volume, while heart rate and blood pressure do not change significantly (Fig. 77.2).

This alteration has several unique features: (a) the augmentation occurs relatively early in pregnancy (20 to 24 weeks); (b) it cannot be explained entirely on the basis of fetal needs; and (c) fluctuations in cardiac output occur with changes in body position as the gravid uterus impinges, to varying degrees, on the inferior vena cava, thus altering systemic venous return (25). Electrocardiographic (ECG) changes observed, but are

| TABLE 77.1 Direct Maternal Deaths, 1991–2008*
<table>
<thead>
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<td>Legal termination</td>
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<tr>
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<td>14°</td>
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<td>11°</td>
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<tr>
<td>Other direct total</td>
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<td>Total number of deaths</td>
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<td>134</td>
<td>106</td>
<td>106</td>
<td>132</td>
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*Deaths reported to the enquiry only and excluding other deaths identified by ONS.

| TABLE 77.2 Indirect Maternal Deaths, 2000–2002*
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<th></th>
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<td>15</td>
<td>16</td>
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<tr>
<td>Other indirect</td>
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<td>86</td>
<td>75</td>
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<td>13</td>
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<tr>
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<td>N/A</td>
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<td>5</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Total number of indirect deaths</td>
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<td>134</td>
<td>136</td>
<td>155</td>
<td>50</td>
<td>49</td>
</tr>
</tbody>
</table>

*Deaths reported to the enquiry only and excluding other deaths identified by ONS.

of no clinical significance, include: sinus tachycardia, left axis deviation, ectopic beats, inverted or flattened T waves, and a Q wave in lead III (26).

**Red Blood Cell, Plasma, and Blood Volume**

An increase of plasma volume is evident by the sixth week of gestation, reaching a value by the end of the first trimester of 15% above that of the nongravid state. There is subsequently a steep increase of this parameter until 28 to 30 weeks of gestation, followed by a more gradual rise, to a final volume at term of 55% above the nonpregnant level (27). Red blood cell mass decreases during the first 8 weeks of gestation due to a decrease in the life span of erythrocytes (23), but increases to nearly 30% above the nonpregnant level at term. These physiologic changes result in a 45% increase of total blood volume and a reduction of the hemoglobin concentration and hematocrit to values of approximately 11.6 g/dL and 35.5 volume %, respectively (Fig. 77.3). Estrogens, progesterone, and placental lactogen elevate aldosterone production either directly or indirectly, and are responsible for the increase of plasma volume during pregnancy. The hyperaldosteronism of pregnancy can result in a progressive decrease in the albumin-to-globulin ratio from approximately 1.5 during pregnancy to 1.1 at term gestation. Maternal colloid osmotic pressure decreases in parallel with the decline in serum albumin concentration from nonpregnant values of 25 to 26 mmHg to approximately 22 mmHg at term. During pregnancy, the glomerular filtration rate (GFR) increases 50% as compared to pregravid levels (28).

**Aortocaval Compression**

Angiographic studies show that the aorta and inferior vena cava can be significantly compressed by the gravid uterus when the woman is in the supine position. In fact, Kerr et al. (29) observed a complete obstruction of the inferior vena cava at term. Although the concentration of globulins declines by 10% during the first trimester, the level rises subsequently to a value at term that is 5% to 10% above the nonpregnant level. These changes result in a progressive decrease in the albumin-to-globulin ratio from approximately 1.5 during pregnancy to 1.1 at term gestation. Maternal colloid osmotic pressure decreases in parallel with the decline in serum albumin concentration from nonpregnant values of 25 to 26 mmHg to approximately 22 mmHg at term. During pregnancy, the glomerular filtration rate (GFR) increases 50% as compared to pregravid levels (28).

**Plasma Proteins, Colloid Osmotic Pressure, and GFR**

The total serum protein concentration decreases from the nonpregnant value of 7.3 to 6.5 g/dL at term gestation. The change is due primarily to a decline of the albumin concentration, which decreases from a nonpregnant level of 4.4 to 3.4 g/dL at term. Although the concentration of globulins declines by 10% during the first trimester, the level rises subsequently to a value at term that is 5% to 10% above the nonpregnant level. These changes result in a progressive decrease in the albumin-to-globulin ratio from approximately 1.5 during pregnancy to 1.1 at term. Maternal colloid osmotic pressure decreases in parallel with the decline in serum albumin concentration from nonpregnant values of 25 to 26 mmHg to approximately 22 mmHg at term. During pregnancy, the glomerular filtration rate (GFR) increases 50% as compared to pregravid levels (28).

**Aortocaval Compression**

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the level of the bifurcation in 80% of women in late pregnancy. Partial obstruction of the aorta at the level of the lumbar for-
dosing (L3–L5) has also been demonstrated in patients between
the 27th week of pregnancy and term gestation (30,31).

The pregnant woman at term, when placed in the lateral
decubitus position, exhibits a right ventricular filling pressure (central venous pressure [CVP]) similar to that of a non-
pregnant woman (32). This observation suggests that venous
return in this position is maintained by the collateral circula-
despite partial caval obstruction (29). In the plain supine
position, however, right atrial pressure falls substantially,
demonstrating that collateral circulation cannot compensate
for complete, or nearly complete, vena cava obstruction (30).
The fall in the cardiac filling pressure that follows this position
change, evident by 20 to 28 weeks of gestation, results in a
decreased stroke volume and cardiac output of approximately
25%, and a 20% reduction of uterine blood flow (33); these are
reliably improved by a tilt to the left of at least 25 degrees (34).

Despite the reduction of cardiac output and stroke volume,
a position change from lateral to supine can be associated with
elevation of blood pressure, resulting from an increase of sys-
temic vascular resistance due to compression of the aorta by
the gravid uterus and enhanced sympathetic nervous system
outflow (35). In approximately 5% of women, however, a sub-
stantial drop in blood pressure occurs (“supine hypotensive
syndrome”), which is associated with bradycardia (usually
following a transient tachycardia) and maternal symptoms of
low systemic perfusion, such as of pallor and sweating, pos-
sibly followed by cardiocirculatory collapse. This occasional,
but profound, drop of venous return may be exacerbated by
neuraxial block, the preferred method of providing anesthe-
sia in pregnant women (36). In conclusion, and based on the
observations above, the intensivist should always consider in
his or her emergency treatment plan the proper positioning of
the pregnant patient and its influence on hemodynamics.

DIAGNOSIS AND TREATMENT

Thrombosis and Thromboembolism
in Pregnancy

Venous thromboembolism (VTE), which includes deep venous
thrombosis (DVT) and pulmonary embolism (PE), occurs in
approximately 1 in 1,000 pregnancies (37). Women are five
times more likely to develop VTE during pregnancy than during
a nonpregnant state (38). Fatal PE, a possible sequela of
VTE, remains a leading cause of maternal mortality in the
Western world (39). The rate of PE in pregnancy is five times
greater than that for nonpregnant women of the same age,
and is about 1 in 100 deliveries; the risks are even higher in
the puerperium.

Risk Factors and Predisposition
to Venous Thrombosis

Compared to nonpregnant women, pregnant women have a
10-fold higher risk of a thrombotic episode. Risk factors for
VTE other than pregnancy are noted in Table 77.4 (40,41).

Pregnancy is associated with an increased clotting potential,
decreased anticoagulant properties, and decreased fibrinolysis.
Pregnancy is accompanied by a two- to threefold increased
concentration of fibrinogen and a 20% to 1,000% increase

| TABLE 77.4 Risk Factors for Venous Thromboembolism (VTE) During Pregnancy |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Cesarean delivery | History of prior VTE | Family history of VTE | Inherited or acquired thrombophilia | Obesity | Older maternal age |
| Higher parity | Prolonged immobilization | | | | |

in factors VII, VIII, IX, X, and XII, all of which peak at term
(42). Levels of von Willebrand factor (vWF) increase up to
400% at term (42). Free protein S levels decline significantly
(up to 35%) during pregnancy due to increased circulating lev-
els of its carrier molecular, complement 4 binding protein (42).
As a consequence, pregnancy is associated with an increase in
resistance to activated protein C (42,43). Levels of plasmino-
gen activation inhibitor-1 (PAI-1) increase three- to fourfold
during pregnancy, while plasma PAI-2 values, negligible before
pregnancy, reach concentrations of 160 mg/L at delivery (35).

Pregnancy is also associated with venous stasis in the lower
extremities, due to compression of the inferior vena cava and
pelvic veins by the enlarging uterus and hormone-mediated
increases—in circulating levels of estrogen and local produc-
tion of prostacyclin and nitric oxide—in deep vein capacitance
secondary. Important hereditary risk factors that can increase
DVT risk are antithrombin III deficiency, protein S and C defi-
ciency, a G1691A mutation of the factor V gene (44), and a
G20210A mutation of the factor II gene (45).

Diagnosis of Venous Thromboembolism
during Pregnancy

Bates and Ginsberg have recently addressed the diagnosis of
VTE during pregnancy in detail (49). In pregnant women
presenting with lower extremity edema, back pain, and/or
chest pain, the prevalence of VTE is less than in the general
population because of the high frequency of these complaints
related to pregnancy. D-dimer assays, which can be used to
exclude VTE in healthy nonpregnant individuals, usually
become positive late in pregnancy, which decreases the utility
of this assay (47). Radiologic studies used to diagnose VTE
in the nonpregnant woman have not been validated in preg-
nancy, and potential risks to the fetus, particularly in terms
of ionizing radiation exposure, need to be considered (48).
Compression ultrasonography (CUS) of the proximal veins
has been recommended as the initial test for suspected DVT
during pregnancy (46). When results are equivocal or an iliac
vein thrombosis is suspected, magnetic resonance venography
(MRV) can be used. MRV does not carry the radiation risk of
contrast venography, and is becoming increasingly available in
the United States.

The approach to the diagnosis of PE is similar in the preg-
nant and nonpregnant individual. Ventilation/perfusion (V/Q)
scanning confers relatively low radiation exposure to the fetus,
a risk less than that of missing a diagnosis of PE in the mother.
However, when a V/Q study is indeterminate in a pregnant
woman without demonstrated lower extremity thrombosis, it
is usually followed by angiography. A brachial approach car-
rries less radiation exposure to the fetus than spiral computed
tomography (CT).
Prevention of Thrombosis during Pregnancy

The optimal anticoagulation regimen has not been established. Low-molecular-weight heparins (LMWHs) have become the anticoagulant of choice because, like unfractionated heparin (UFH), they do not cross the placenta, have better bioavailability, and carry less risk of osteoporosis and heparin-induced thrombocytopenia than UFH (49,50). A recent review of published data on the use of LMWHs in pregnancy supports their use as safe alternatives to UFH as anticoagulants during pregnancy (51). A more recent practice trend, especially in the United States, has been to switch patients to the longer-acting, subcutaneous UFH a few weeks before delivery to allow the use of activated partial thromboplastin time (aPTT) as a diagnostic test to assess anticoagulation pre- and postlabor (52).

Another means of providing VTE prophylaxis is with elastic compression stockings, which may be used for the entire pregnancy. Elastic stockings are appropriate for in-hospital patients at increased risk of VTE, and may be combined with the use of LMWH. Vena cava filter placement represents a potentially important, but poorly evaluated, therapeutic modality in the prevention of pulmonary emboli. Randomized trials to establish the appropriate role of vena cava filters in the treatment of venous thromboembolic disease are lacking (53).

Thrombolytic Therapy for Pulmonary Embolism

The indications for thrombolytic therapy for PE remain controversial. The incidence of intracranial hemorrhage may be as high as 2% to 3% with systemic thrombolytic therapy (54), although rates were lower in a recent trial (55). Fatality rates in patients with PE presenting in cardiogenic shock may be as high as 30% (54); thrombolytic therapy should be considered in this circumstance, although evidence for this subgroup is limited (56). Approximately 10% of symptomatic pulmonary emboli are rapidly fatal (57,58). The International Cooperative Pulmonary Embolism Registry, established to ascertain PE mortality, reported that 2% of patients were first diagnosed with PE at autopsy (59). Of patients diagnosed with PE before death, 5% to 10% have shock at presentation, which is associated with a mortality of 25% to 50% (59–61).

Echocardiographic evidence of right ventricular dysfunction at presentation also has been suggested as an indication for thrombolytic therapy (55); however, a recent randomized trial failed to demonstrate a survival benefit with thrombolysis in patients with this finding (55), and mortality rates with conventional therapy are conflicting (54). At the time of this writing, routine thrombolysis cannot be justified in all patients.

Hemorrhage

Peripartum hemorrhage (PPH) remains a significant cause of maternal and fetal morbidity and mortality. In the United States and other industrialized nations, massive obstetric hemorrhage has generally ranked among the top three causes of maternal death despite modern improvements in obstetric practice and transfusion services.

PPH includes a wide range of pathophysiologic events. Antepartum bleeding occurs in nearly 4% of pregnant women (62). The causes of serious antepartum bleeding are abnormal implantation (placenta previa, placenta accreta), placental abruption, or uterine rupture. The latter is often caused by a dehiscence of a pre-existing uterine scar. The main reason for postpartum bleeding is uterine atony when myometrial contraction is inadequate. It is not surprising that uterine bleeding may be fatal when considering the massive amount of blood flow perfusing the uterus at term (up to 600 mL/min). Patients with hemodynamic instability or massive hemorrhage require prompt resuscitative measures, including the administration of supplemental oxygen, placement of at least two large bore* intravenous lines, intravenous hydration with isotonic crystalloid, and blood typing and cross-matching for the replacement of packed red blood cells (Table 77.5). A delay in the correction of hypovolemia, diagnosis and treatment of impaired coagulation, or surgical control of bleeding are the avoidable factors in most maternal mortality cases caused by hemorrhage. If a transfusion must be given before full cross-matching is finished, type-specific uncross-matched blood can be used (63); alternatively, if there is no cross-matched blood, type O, Rh negative blood may be used in an emergency. Several recent studies suggest that fibrinogen is an important predictor of severe PPH (64,65). Standard coagulation screening tests such as the prothrombin time, partial thromboplastin time, and fibrinogen concentration have been supplemented or replaced by global coagulation tests such as thromboelastography (TEG) or rotational thrombelastography (ROTEM) (66).

There is virtually unanimous agreement from professional societies on the need of multidisciplinary hemorrhage protocols for management of both trauma and PPH (67–69). Such protocols ensure rapid availability of prepared blood products and a concomitant reduction in the time to transfusion and resuscitation. If the placenta has not been delivered when hemorrhage begins, it should be removed, if necessary by manual exploration of the uterine cavity. Placenta accreta is diagnosed if the placental cleavage plane is indistinct. In this situation, the patient should be prepared by the intensivist or the anesthesiologist for probable urgent hysterectomy. Firm bimanual

<table>
<thead>
<tr>
<th>TABLE 77.5 Management of Severe Postpartum Hemorrhage</th>
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<td><strong>Conservative Management</strong></td>
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<td>General Measures</td>
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<tr>
<td>• Administration of supplemental oxygen</td>
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<td>• Placement of adequate intravenous access lines</td>
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<tr>
<td>• Intravenous hydration</td>
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<tr>
<td>• Blood typing and cross-matching</td>
</tr>
<tr>
<td>• Placement of arterial line for repeated blood sampling</td>
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<td>Pharmacologic Measures</td>
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<td>• Methylergonovine</td>
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<td>• 15-Methyl prostaglandin F_{2α}</td>
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<td><strong>Surgical Management</strong></td>
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<tr>
<td>Hysterectomy</td>
</tr>
<tr>
<td>• Supracervical</td>
</tr>
<tr>
<td>• Total</td>
</tr>
</tbody>
</table>

*Remember that resistance to flow is proportional to the fourth power of the radius of an orifice. Thus a shorter, larger catheter is preferred, whether peripheral or central. A 14-gauge 1.25-in peripheral IV or a 7-French (Fr) peripheral introducer may be used, as may a 9- to 12-Fr 15 cm (length) central introducer.
compression of the uterus (with one hand in the posterior vaginal fornix and the other on the abdomen) can limit hemorrhage until help can be obtained. Hemorrhage after placental delivery should prompt vigorous fundal massage while the patient is rapidly given 10 to 30 units of oxytocin in 1 L of intravenous crystalloid. Uterotonic agents such as oxytocin are routinely used in the management of uterine atony (70). This synthetic nonpeptide is a first-line therapeutic agent because of the paucity of side effects and the absence of contraindications. If the fundus does not become firm, uterine atony is the presumed (and most common) diagnosis. Although fundal massage continues, the patient may be then given 0.2 mg of methylergonovine (Methergine) intramuscularly, with this dose to be repeated at 2- to 4-hour intervals if necessary. Methylergonovine, an ergot alkaloid, is used as a second-line uterotonic agent in the setting of massive obstetric hemorrhage due to uterine atony. It may cause undesirable adverse effects such as cramping, headache, and dizziness. Coexisting severe hypertension is an absolute contraindication to its use.

Injectable prostaglandins may also be used when oxytocin fails. Both prostaglandin E and prostaglandin F2 stimulate myometrial contractions, and have been used intramuscularly or intravenously for refractory hemorrhage due to uterine atony. In particular, carboprost (Hemabate), 15-methyl prostaglandin F2-α, may be administered intramuscularly or intramyometrially in a dosage of 250 μg every 15 to 90 minutes, up to a maximum dosage of 2 mg. Sixty-eight percent of patients respond to a single carboprost injection; 86% respond to a second dose (71). Because oxygen desaturation has been reported with the use of carboprost (72), patients should be monitored by pulse oximetry.

The use of a hydrostatic balloon has been advocated as an alternative to uterine packing for controlling hemorrhage due to uterine atony (73). The inflated Rusch balloon can conform to the contour of the uterine cavity and provides an effective tamponade. Life-threatening hemorrhage can also be treated via arteriolar embolization by interventional radiology (74). Finally, in cases of continuing hemorrhage, a variety of surgical techniques can be used to avoid a hysterectomy, such as bilateral uterine artery ligation or internal iliac ligation (75).

Amniotic Fluid Embolism

Although the entry of amniotic fluid into the maternal circulation was already recognized as early as 1926 (76), Morgan published the first major review on the topic in 1979 (77). He reviewed 272 cases reported in the English language literature to that date. Although the true incidence of this disease entity is not known, most authors estimate it to be between 1 in 8,000 and 1 in 80,000 pregnancies.

Clinical Presentation

The classic presentation of amniotic fluid embolism is described as a sudden, profound, and unexpected cardiovascular collapse followed, in many cases, by irreversible shock and death (78). The only known predisposing factor to this life-threatening complication of pregnancy appears to be multiparity, seen with 88% of cases (77). In a smaller percentage of cases (51%), the presenting symptom is respiratory related. Hypotension is present in 27% of surviving cases, with coagulopathy comprising 12% and seizures 10%. Fetal bradycardia (17%) and hypotension (13%) are the next most common presenting features (Table 77.6).

Etiology and Pathophysiology

A common misperception in the literature is that the entry of amniotic fluid into maternal circulation is routine. This belief arises from the recognized presence of squamous cells in the pulmonary vasculature as a marker signaling the entry of amniotic fluid into the maternal circulation. Studies have now shown that squamous cells can appear in the pulmonary blood of heterogenous populations of both pregnant and nonpregnant patients who have undergone pulmonary artery (PA) catheterization (79–83); the presence of these cells is probably the result of contamination by epithelial cells derived from the cutaneous entry site of the device (79,80). Because it is difficult to differentiate adult from fetal epithelial cells, the isolated finding of squamous cells in the pulmonary circulation of pregnant patients, with or without coexisting thrombotic PE, should be seen as a contaminant and not indicative of maternal exposure to amniotic fluid (84–86).

It has been hypothesized that amniotic fluid could act as a direct myocardial depressant. In vitro observation shows that amniotic fluid can cause a decrease in myometrial contractility (87). Other humoral factors, including proteolytic enzymes, histamine, serotonin, prostaglandins, and leukotrienes, may contribute to the hemodynamic changes and consumptive coagulopathy associated with amniotic fluid embolus, with a pathophysiologic mechanism similar to distributive or anaphylactic shock (87,88).

Diagnosis and Management

Amniotic fluid embolus syndrome is a diagnosis of exclusion (Table 77.7), and the treatment is essentially supportive. Hemodynamic instability should be treated with optimization of preload by rapid volume infusion. An α-receptor agonist, such as phenylephrine, may be useful to maintain adequate aortic perfusion pressure (90 mmHg systolic) while volume is infused. Coagulopathy associated with amniotic fluid embolus should be treated with aggressive administration of blood component therapy. If maternal cardiopulmonary resuscitation (CPR) must be initiated, and the fetus is sufficiently mature and is undelivered at the time of the cardiac arrest, a perimortem cesarean section should be immediately instituted (88–90).

### TABLE 77.6 Clinical Presentation of Amniotic Fluid Embolism

- Acute cardiorespiratory collapse
- Acute respiratory distress
- Hypotension
- Hemorrhage/coagulopathy
- Seizures
- Fetal distress

### TABLE 77.7 Differential Diagnosis of Amniotic Fluid Embolus

- Thrombosis
- Air embolus
- Septic shock
- Acute myocardial infarction
- Peripartum cardiomyopathy
- Anaphylaxis
- Aspiration
- Placental abruption
- Transfusion reaction
- Local anesthetic toxicity
Peripartum Cardiomyopathy

PPCM, a rare disease of unknown cause that strikes women in the childbearing years, is associated with a high mortality rate. PPCM is defined by the development of left ventricular or biventricular failure in the last month of pregnancy or within 5 months of delivery in the absence of other identifiable cause (91). In the United States, PPCM can affect women of various ethnic backgrounds at any age, but is more common in women 30 years of age or older. The strong association of PPCM with gestational hypertension and twin pregnancy should raise the level of suspicion for this condition in pregnant patients who develop symptoms of congestive heart failure (92).

Etiology and Diagnosis

A number of possible causes have been proposed for PPCM, including myocarditis (93), abnormal immune response to pregnancy, maladaptive response to the hemodynamic stresses of pregnancy (94), stress-activated cytokines, and prolonged tocolysis. A genetic tract is probable, as there have been reported few cases of familial PPCM. The diagnosis of PPCM requires the exclusion of more common causes of cardiomyopathy, and should be confirmed by standard echocardiographic assessment of the left ventricular systolic dysfunction, including depressed fractional shortening and ejection fraction documentation (95,96). PPCM shows many clinical characteristics of dilated cardiomyopathy (DCM) (97). Although the two conditions likely share part of their pathogenesis, such as predisposing mutations, increased oxidative stress, impaired microvasculature, and damaged sarcomere integrity, the exact underlying pathways might be differently altered in PPCM and DCM.

Treatment and Prognosis

Therapy should be initiated using standard clinical protocols for heart failure, although angiotensin-converting enzyme inhibitors should be avoided prenatally. Long-term clinical prognosis is usually defined within 6 months after delivery (98). In one study, approximately half of 27 women studied had persistent left ventricular dysfunction beyond 6 months, with a cardiac mortality rate of 85% over 5 years, as compared with the group in whom cardiac size returned to normal by the same time interval, with no mortality (91). The identification of the underlying cause of heart failure in the pregnant woman is another important factor that influences long-term survival (99). It is critical to note that the risk of recurrence with future pregnancies is particularly high in women with persistent left ventricular dysfunction prior to their subsequent pregnancy (100).

Hypertensive Disease of Pregnancy

Diagnosis

Preeclampsia complicates around 5% of pregnancies and, worldwide, hypertensive disorders of pregnancy are responsible for over 60,000 maternal deaths annually (101). Hypertensive disorders of pregnancy include chronic hypertension, preeclampsia/eclampsia, preeclampsia superimposed on chronic hypertension, and gestational hypertension (102). Preeclampsia is a pregnancy-specific, multisystem disorder that is characterized by the development of hypertension and proteinuria after 20 weeks of gestation (103). The disorder complicates approximately 5% to 7% of pregnancies (104), with an incidence of 23.6 cases per 1,000 deliveries in the United States (105). Chronic hypertension is defined by elevated blood pressure that predates the pregnancy, and is documented before 20 weeks of gestation or is present 12 weeks after delivery. Eclampsia, a severe complication of preeclampsia, is a new onset of seizures in women with preeclampsia.

Diagnostic criteria for preeclampsia include new onset of elevated blood pressure and proteinuria after 20 weeks of gestation. Severe preeclampsia is indicated by more substantial blood pressure elevations and a greater degree of proteinuria. Other features of severe preeclampsia include oliguria, cerebral or visual disturbances, and pulmonary edema or cyanosis (Table 77.8) (102,106).

Therapy

A major goal toward improving antenatal management of preeclampsia is to develop accurate prediction models that identify women at high risk of disease. Initial therapeutic goals during labor are focused on preventing seizures and controlling hypertension (106). Magnesium sulfate is the medication of choice to prevent eclamptic seizures for either preeclampsia or eclamptic seizures (107). Magnesium sulfate has been shown to be superior to phenytoin (Dilantin) and diazepam (Valium) for the treatment of eclamptic seizures, although magnesium does not prevent the progression of the disorder (108,109). Women with systolic blood pressures of 160 to 180 mmHg, or higher diastolic blood pressures of 105 to 110 mmHg should receive immediate antihypertensive therapy. The treatment goal is to lower systolic pressure to 140 to 150 mmHg and diastolic pressure to 90 to 100 mmHg. Hydralazine (Apresoline) and labetalol (Normodyne, Trandate) are the antihypertensive drugs most commonly used. Nifedipine (Procardia) and sodium nitroprusside (Nitropress) are potential alternatives, but their use is associated with significant adverse effects and risk of overdose. Similarly, labetalol should not be used in women with asthma or congestive heart failure. Angiotensin-converting enzyme inhibitors are also contraindicated in this

<table>
<thead>
<tr>
<th>TABLE 77.8 Physical Examination of the Severely Preeclamptic Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Funduscopic</strong></td>
</tr>
<tr>
<td>• Arteriolar spasm (focal or diffuse)</td>
</tr>
<tr>
<td>• Retinal edema</td>
</tr>
<tr>
<td>• Retinal hemorrhages (superficial and flame shaped, or deep</td>
</tr>
<tr>
<td>and punctate)</td>
</tr>
<tr>
<td>• Retinal exudates (hard or “cotton wool”)</td>
</tr>
<tr>
<td>• Papilledema</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
</tr>
<tr>
<td>• Heart failure (rales, elevated jugular venous pressure, S3)</td>
</tr>
<tr>
<td>• Aortic dissection</td>
</tr>
<tr>
<td>• New or increased murmur of mitral regurgitation</td>
</tr>
<tr>
<td>• Bruits</td>
</tr>
<tr>
<td><strong>Neurologic</strong></td>
</tr>
<tr>
<td>• Hypertensive encephalopathy: Disorientation</td>
</tr>
<tr>
<td>• Depressed consciousness (Glasgow coma scale score &lt;13)</td>
</tr>
<tr>
<td>• Focal deficits, generalized or focal seizures</td>
</tr>
<tr>
<td><strong>Abdominal</strong></td>
</tr>
<tr>
<td>• Palpation for liver tenderness or increase in size</td>
</tr>
<tr>
<td><strong>Fetal</strong></td>
</tr>
<tr>
<td>• Assessment of fetal well-being (fetal heart rate strip, biophysical profile)</td>
</tr>
</tbody>
</table>
group of patients as they may cause birth defects (110). In women with preeclampsia, blood pressure usually normalizes within a few hours after delivery but may remain elevated for 2 to 4 weeks (111).

**Care and Management of the Hypertensive Parturient**

Some patients with severe preeclampsia will require intensive care unit (ICU) admission for invasive monitoring and close supervision. Typical indications include (a) a severe increase in blood pressure, with diastolic blood pressures greater than 115 to 120 mmHg or a systolic blood pressure greater than 200 mmHg, refractory to initial antihypertensive therapy; (b) oliguria refractory to repeated fluid challenges; (c) eclamptic seizures; or (d) respiratory insufficiency. The initial physical examination should include a neurologic assessment, fundoscopic examination, auscultation of the heart and lungs, and palpation of the abdomen (see Table 77.8). If magnesium sulfate is given, it should be continued for 24 hours following delivery or for at least 24 hours after the last seizure. Regular assessment of urine output, maternal reflexes, respiratory rate, and oxygen saturation is paramount while magnesium is infused. A loading dose of 4 g should be given by infusion pump over 5 to 10 minutes, followed by a further infusion of 1 g/hr maintained for 24 hours after the last seizure. Gradual antihypertensive therapy can be accomplished with a 25% reduction of mean arterial pressure within minutes to 2 hours, to 160/100 mmHg (Table 77.9) (112).

Most patients satisfying the criteria for ICU admission should be monitored with central venous access and an arterial catheter. The use of invasive monitoring facilitates therapeutic goals and can clarify the suspected diagnosis. Although, occasionally, the use of a PA catheter facilitates cardiovascular management by monitoring cardiac output and systemic oxygen delivery while gradually reducing systemic vascular resistance and restoring preload, recent advances in noninvasive cardiac output measurement devices have been validated and may be used to monitor the effect of therapeutic interventions (113).

**Fetal Monitoring in the Intensive Care Setting**

Electronic fetal monitoring (EFM) is used in the management of labor and delivery in nearly three of four pregnancies in the United States. The apparent contradiction between the widespread use of EFM and expert recommendations to limit its routine use indicates that a reassessment of this practice is warranted (114). Even more difficult is the question of whether fetal monitoring is of any substantial use in the critically ill mother or the mother undergoing surgery. Continuous cardiotocography (CTG) during labor is associated with a reduction in neonatal seizures, but no significant differences in cerebral palsy, infant mortality, or other standard measures of neonatal well-being. On the contrary, this monitoring technique was associated with an increase in cesarean sections and instrument-aided vaginal births. When considering the use of EFM, the intensivist should consider the effects of many sedative, hypnotic, or analgesic drugs routinely used in the critical care setting on fetal heart rate variability (115–117). At this time, no systematic studies have been performed concerning the value of CTG during general anesthesia for nonobstetric surgery; it is assumed that uneventful sedation and analgesia provide adequate oxygenation and circulatory stability without having any influence on the fetus (115–117).

**TABLE 77.9 Antihypertensive Therapy in Preeclampsia**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial dose</th>
<th>Maintenance</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol (Normodyne, Trandate)</td>
<td>5 mg IV</td>
<td>5–10 mg IV q20–30min</td>
<td>Avoids reflex tachycardia</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>Start at 10 μg/min to 400 μg/min until desired effect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydralazine (Apresoline)</td>
<td>5 mg IV</td>
<td>Maintenance: 5–10 mg IV q20–30min</td>
<td></td>
</tr>
<tr>
<td>Other antihypertensive options</td>
<td>Nicardipine, nitroprusside, phentolamine, fenoldopam, diazoxide</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Pulmonary Edema in Pregnancy**

Pulmonary edema is a rare, but well-documented, complication of tocolytic therapy in pregnant women (118–120). The incidence of pulmonary edema related to β-mimetic tocolysis is estimated to be 0.15% (121). The etiology of the pulmonary edema is unclear, but is likely multifactorial (122), and both cardiogenic and noncardiogenic mechanisms have been proposed. Possible cardiogenic causes include fluid overload, catecholamine-related myocardial necrosis, cardiac failure secondary to reduced diastolic compliance, and down-regulation of β-receptors (121–125).

**Treatment**

Immediate recognition and appropriate therapy can ameliorate the course of respiratory insufficiency in patients who develop pulmonary edema during tocolytic treatment. Therapy involves discontinuing the medication, ensuring adequate ventilation and oxygenation, correcting fluid imbalance and hypotension, and maintaining adequate cardiac output. Continuous assessment of the fetus’ well-being is necessary.

**Tocolytic Therapy**

The development of pulmonary edema during the course of β-adrenergic agonist treatment for preterm labor is an indication for discontinuing the treatment and either switching to a different type of labor-inhibiting drug or terminating all efforts to prevent preterm delivery. Magnesium sulfate, calcium channel blockers, or oxytocin antagonists are the most frequently used alternatives.

**Venticulatory Support**

This topic is reviewed extensively in other sections of the book. Mechanical ventilation principles are not different for the pregnant woman, and are being standardized by evidence-based medicine and consensus conferences (125–127).

**Fetal Considerations**

Fetal well-being must be interpreted within the context of maternal respiratory failure. Minimally, intermittent fetal monitoring is indicated. If refractory maternal hypoxemia and acidosis presents, and results in fetal distress, cesarean delivery to salvage the fetus should be considered.
Cardiopulmonary Resuscitation in Pregnancy

The major causes of maternal cardiac arrest are due to trauma, cardiac conditions, and embolism. Other causes are sepsis, magnesium overdose, complications of eclampsia, or the result of an unanticipated difficult intubation. The general treatment of the pregnant woman in cardiac arrest is no different than any other patient, including drug dosages and defibrillation settings. Chest compressions and ventilations should be performed with the recommended sequence. Because a slight left tilt of the pregnant patient during CPR enhances venous return after 24 weeks of gestation, this position is recommended (90,128,129). Because of reduced pulmonary reserve, pregnant women do not tolerate hypoxia well. IV fluid should be running wide open on pressure bags, and blood products should be considered if hemorrhage is suspected. Once the age of the fetus is determined, a decision can be made whether to proceed with a perimortem cesarean section. The fetus can tolerate hypoxia longer than normal, but the decision to proceed with a cesarean delivery should be made within 4 minutes (126). In a recent retrospective review on CPR with perimortem cesarean section, authors found 35 reports with 20 potentially resuscitable causes, of which 13 women survived (127). Although this recent review fell short of proving that perimortem cesarean delivery within 4 minutes of maternal cardiac arrest improves maternal and neonatal outcomes, it provided additional support for this procedure. An extensive review of this topic is also available on the American Society of Anesthesiologists (ASA) website (130).

Anesthesiologists have recognized that the management of the airway in the obstetric patient may be especially challenging. According to the closed claims analysis of the ASA, the main mechanisms for airway problems are inadequate ventilation, esophageal intubation, and difficult intubation (131). If the anesthesiologist encounters an unanticipated difficult airway, alternative airway management attempts may include the laryngeal mask airway (LMA) or the Combitube. If cricothy- way, alternative airway management attempts may include the anesthesiologist encounters an unanticipated difficult intubation, esophageal intubation, and difficult intubation (131). If main mechanisms for airway problems are inadequate ventilation. According to the closed claims analysis of the ASA, the airway in the obstetric patient may be especially challenging. Although this recent review fell short of proving that perimortem cesarean delivery within 4 minutes of maternal cardiac arrest improves maternal and neonatal outcomes, it provided additional support for this procedure. An extensive review of this topic is also available on the American Society of Anesthesiologists (ASA) website (130). Anesthesiologists have recognized that the management of the airway in the obstetric patient may be especially challenging. According to the closed claims analysis of the ASA, the main mechanisms for airway problems are inadequate ventilation, esophageal intubation, and difficult intubation (131). If the anesthesiologist encounters an unanticipated difficult airway, alternative airway management attempts may include the laryngeal mask airway (LMA) or the Combitube. If cricothyrotomy becomes necessary, this maneuver should be initiated in a timely fashion to minimize the chance of maternal hypoxic brain damage.

SUMMARY

The obstetric patient poses exceptional challenges to the ICU team. Knowledge of the physiologic changes of pregnancy and specific pregnancy-related disorders is necessary for optimal management. The critically ill obstetric patient is unique in terms of medical management and often requires the input of several specialties. These patients require specialized nursing care and aggressive monitoring of both mother and fetus, and often include invasive monitoring of the mother. ICU diagnoses may include preeclampsia, including the HELLP (Hemolysis, Elevated Liver enzymes, Low Platelets) syndrome, pulmonary embolic disease, anemotic fluid embolism, status asthmaticus, respiratory infection, acute respiratory distress syndrome, and sepsis. Although there is little doubt that intensivists in an ICU can best treat these patients, the maternal–fetal medicine physician should be included in the treatment team. The management of mechanical ventilation is based on modern principles of avoiding lung injury, while hypercapnia may be tolerated even during the pregnancy. Care must include the consideration of pregnancy-induced physiologic changes, normal laboratory alterations, and continued fetal well-being if antepartum. Ultimately, the goal of this interdisciplinary approach is to ensure cohesive coordinated care for the pregnant woman.

Key Points

- The pregnant woman undergoes important physiologic changes: minute ventilation increases leading to a compensated respiratory alkalosis. The ERV is decreased and the time to desaturation with apnea decreases. Cardiac output increases up to 45%, which can be primarily attributed to an increase in stroke volume. The aorta and inferior vena cava can be significantly compressed by the gravid uterus in the supine position resulting in supine hypotension in up to 5% of term pregnant women.
- Compared to nonpregnant women, pregnant women have a 10-fold risk of a thrombotic episode and thromboembolic events are the leading causes of death in developed countries.
- Other important diagnoses leading to an intensive care admission are eclampsia, congenital or acquired cardiac diseases or pulmonary edema.

References


