CHAPTER 47: Critical Care and Trauma

The pregnant women is exposed to the same possibility of injury as at other times, the prognosis not being naturally altered except that abortion frequently occurs.

—J. Whitridge Williams (1903)

INTRODUCTION

These observations made more than a century ago are less applicable today to critically ill pregnant women because of current intensive care capabilities. For example, severe medical, surgical, and obstetrical disorders complicating pregnancy are frequently managed by a multidisciplinary team for optimal care. It is axiomatic that obstetricians and other members of the health-care team must have a working knowledge of the unique considerations for pregnant women. Some of those discussed in Chapter 46 include pregnancy-induced physiological changes, alterations in normal laboratory values, and consideration for the second patient—the fetus. Because these critically ill women are usually young and in good health, their prognosis is generally better than that of many other patients admitted to intensive care units (ICUs) (Gaffney, 2014).

OBSTETRICAL INTENSIVE CARE

In the United States each year, 1 to 3 percent of pregnant women require critical care services, and the risk of death during such admissions ranges from 2 to 11 percent (American College of Obstetricians and Gynecologists, 2017b). Those with pregnancy-associated complications—especially hemorrhage and hypertension—have the greatest need for intensive care (Chantry, 2015; Gaffney, 2014; Guntupalli, 2015a,b). That said, many antepartum admissions are for nonobstetrical reasons, and these include diabetes, pneumonia or asthma, heart disease, chronic hypertension, pyelonephritis, and thyrotoxicosis (Guntupalli, 2015b; Zeeman, 2006). Additionally, intrapartum and postpartum critical care for hypertensive disorders, hemorrhage, sepsis, or cardiopulmonary complications is often required. In instances of life-threatening hemorrhage, surgical procedures may be necessary, and close proximity to a delivery-operating room is paramount. For women who are undelivered, fetal well-being is also better served by this close proximity, especially because many are delivered preterm (Kilpatrick, 2016).

Organization of Critical Care

The concept and development of critical care for all aspects of medicine and surgery began in the 1960s. The National Institutes of Health held a Consensus Conference (1983) and the Society of Critical Care Medicine (1988, 1999) subsequently established guidelines for ICUs. Especially pertinent to obstetrics, these costly units prompted the evolution of a step-down *intermediate care unit*. These latter units were designed for patients who did not require intensive care, but who needed a higher level of care than that provided on a general ward. The American College of Critical Care Medicine and the Society of Critical Care Medicine (1998) have published guidelines for these units (Table 47-1).

TABLE 47-1

Guidelines for Conditions That Could Qualify for Intermediate Care

Cardiac: evaluation for possible infarction, stable infarction, stable arrhythmias, mild-to-moderate congestive heart failure, hypertensive urgency without end-organ damage
Pulmonary: stable patients for weaning and chronic ventilation, patients with potential for respiratory failure who are otherwise stable
Neurological: stable central nervous system, neuromuscular, or neurosurgical conditions that require close monitoring
Drug overdose: hemodynamically stable
Gastrointestinal: stable bleeding, liver failure with stable vital signs
Endocrine: diabetic ketoacidosis, thyrotoxicosis that requires frequent monitoring
Surgical: postoperative from major procedures or complications that require close monitoring
Miscellaneous: early sepsis, patients who require closely titrated intravenous fluids, pregnant women with severe preeclampsia or other medical problems

Data from Nasraway, 1998.

Obstetrical Critical Care

Although the evolution of critical care for obstetrical patients has generally followed developments just described, there are no specific guidelines. Most hospitals employ a blend of these concepts, and in general, units can be divided into three types.

First, in most hospitals, severely ill women are transferred to medical or surgical ICUs that are operated by specialists often certified in critical care medicine. Admissions or transfers to these units are situation-specific and based on the acuity of care needed and on the ability of the facility to provide it. For example, pregnant women who require ventilatory support, invasive monitoring, or pharmacological support of circulation are typically transferred to an ICU (Chantry, 2015). Another example is the neurological ICU (Sheth, 2012). In an earlier review of more than 25 tertiary-care referral institutions, approximately 0.5 percent of obstetrical patients were transferred to these types of ICUs (Zeeman, 2006).

A second type is the obstetrical intermediate care unit, sometimes referred to as a high-dependency care unit (HDU). One example is found at Parkland Hospital. Located within the labor and delivery unit, it has designated rooms staffed by experienced personnel. The two-tiered system incorporates the guidelines for intermediate and intensive care. Care is provided by maternal-fetal medicine specialists and nurses with experience in critical care obstetrics. As needed, this team is expanded to include other obstetricians and anesthesiologists, hospitalists, gynecological oncologists, pulmonologists, cardiologists, surgeons, and other medical and surgical subspecialists (Stevens, 2015). Many tertiary-care centers have developed similar intermediate care units and use selected triage to ICUs. Guidelines for such transfers must follow the federal Emergency Medical Treatment and Labor Act (EMTALA) guidelines. According to the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists (2017), the minimal monitoring required for a critically ill patient during transport includes continuous pulse oximetry, electrocardiography, and regular assessment of vital signs. They must have secure venous access, and those who are mechanically ventilated must have endotracheal tube position confirmed and secured. Left uterine displacement and supplemental oxygen is applied routinely during transport of antepartum patients. Continuous fetal heart rate or tocodynamic monitoring is individualized.

Last, obstetrical ICUs are full-care ICUs but are operated by obstetrical and anesthesia personnel in the labor and delivery unit. Only a few obstetrical services have these capabilities (Zeeman, 2003, 2006).

For smaller hospitals, transfer to a medical or surgical ICU is usually preferable, and sometimes transfer to another hospital is necessary. As discussed,

indications for admission to these types of critical care units vary, however, patient mix for these units is similar (Table 47-2). The American College of Obstetricians and Gynecologists (2017b) has summarized critical obstetrical care implementation depending on hospital size and technical facilities.

TABLE 47-2

Comparison of Acuity of Patient Mix for Obstetrical Critical Care Shown in Percent

Factor	Intermediate Care Unit (n = 483)[a]	Medical-Surgical ICU (n = 813)[b]
Stage		
Antepartum	20	23
Postpartum	80	77
Indication[c]		
Hypertension	45	40
Hemorrhage	18	21
Cardiopulmonary	12	16
Sepsis	5	8
Pregnancy-Related Mortality	0.2	2

[a]Data from Zeeman, 2003.

[b]Data from Baskett, 2009; Keizer, 2006; Paxton, 2014; Small, 2012; Stevens, 2006; Vasquez, 2007.

[c]Columns of indications do not total 100 percent because some diagnoses are not listed.

Pulmonary Artery Catheter

Data obtained during pregnancy with pulmonary artery catheterization (PAC) have contributed immensely to the understanding of normal pregnancy hemodynamics and pathophysiology of common obstetrical conditions. These include preeclampsia-eclampsia, acute respiratory distress syndrome, and amnionic-fluid embolism (Clark, 1988, 1995, 1997; Cunningham, 1986, 1987; Hankins, 1984, 1985). Also, because of these studies, most have concluded that such monitoring is seldom necessary (American College of Obstetricians and Gynecologists, 2013; Gidwani, 2013; Magder, 2015).

In nonobstetrical patients, randomized trials of nearly 5000 subjects have shown no benefits with PAC (Harvey, 2005; National Heart, Lung, and Blood Institute, 2006; Sandham, 2003). According to a Cochrane Database review, no randomized trials have used PAC for preeclampsia management (Li, 2012). The overall mechanisms, benefits, and risks were recently reviewed by Magder (2015).

Hemodynamic Changes in Pregnancy

Formulas for deriving some hemodynamic parameters are shown in Table 47-3. These measurements can be indexed for body size by dividing by body surface area (BSA). Normal values for nonpregnant adults are used, but with the caveat that these may not necessarily reflect changes induced by the more “passive” uteroplacental perfusion.

TABLE 47-3

Formulas for Deriving Various Cardiopulmonary Parameters

Mean arterial pressure (MAP) (mm Hg) = [SBP + 2 (DBP)] ÷ 3
Cardiac output (CO) (L/min) = heart rate × stroke volume
Stroke volume (SV) (mL/beat) = CO/HR
Stroke index (SI) (mL/beat/m2) = stroke volume/BSA
Cardiac index (CI) (L/min/m2) = CO/BSA
Systemic vascular resistance (SVR) (dynes × sec × cm−5) = [(MAP − CVP)/CO] × 80
Pulmonary vascular resistance (PVR) (dynes × sec × cm−5) = [(MPAP − PCWP)/CO] × 80

BSA = body surface area (m^2); CVP = central venous pressure (mm Hg); DBP = diastolic blood pressure; HR = heart rate (beats/min); MAP = mean systemic arterial pressure (mm Hg); MPAP = mean pulmonary artery pressure (mm Hg); PCWP = pulmonary capillary wedge pressure (mm Hg); SBP = systolic blood pressure.

In a landmark investigation, Clark and colleagues (1989) used PAC to obtain cardiovascular measurements in healthy pregnant women and again in these same women when nonpregnant (Chap. 4, Hemodynamic Function in Late Pregnancy). Because increased blood volume and cardiac output are compensated by decreased vascular resistance and increased pulse rate, ventricular performance remains within the normal range at term.

Cardiac complications are a common indication for ICU admission of pregnant women (Guntupalli, 2015b). Evaluation of cardiac function is frequently performed using echocardiography. This technology is indispensable in interrogating cardiac anatomy and especially right-ventricular function (Krishnan, 2015; Thiele, 2015). It is considered in more detail in Chapter 49 (Peripartum Management Considerations), and some normal values are listed in the Appendix (Maternal Echocardiographic Measurements). A working knowledge of cardiovascular physiology in pregnancy is paramount to understanding the pathophysiology of gestational complications discussed later in this chapter and throughout the book.

ACUTE PULMONARY EDEMA

The incidence of pulmonary edema complicating pregnancy averages 1 in 500 deliveries at tertiary referral centers. The two general causes are: (1) *cardiogenic,* namely, hydrostatic edema caused by high pulmonary capillary hydraulic pressures, and (2) *noncardiogenic,* that is, permeability edema caused by capillary endothelial and alveolar epithelial damage. In pregnancy, noncardiogenic pulmonary edema is more common. Taken in toto, studies in gravidas indicate that more than half who develop pulmonary edema have some degree of sepsis syndrome in conjunction with tocolysis, severe preeclampsia, or obstetrical hemorrhage combined with vigorous fluid therapy (O'Dwyer, 2014; Thornton, 2011).

Although cardiogenic pulmonary edema is less frequent, common precipitating causes include resuscitation for hemorrhage and vigorous treatment of preterm labor. In one study, the causes in 51 women with pulmonary edema were cardiac failure, tocolytic therapy, iatrogenic fluid overload, and preeclampsia (Sciscione, 2003). In another study, more than half of cases were associated with preeclampsia, and the other three causes had equal distribution (Hough, 2007). In still another study of 53 cases, 83 percent were caused by hypertensive disorders, 11 percent cardiac, and 6 percent sepsis (O'Dwyer, 2015). Although used less commonly today, tocolytic therapy with β-mimetic drugs at one time was the cause of up to 40 percent of pulmonary edema cases (DiFederico, 1998; Gandhi, 2014; Jenkins, 2003).

Noncardiogenic Permeability Edema

Endothelial activation is the common denominator that is associated with preeclampsia, sepsis syndrome, and acute hemorrhage—or frequently combinations thereof—and they are the most common predisposing factors to pulmonary edema (Table 47-4). As discussed, these clinical scenarios

are often associated with corticosteroids given to induce fetal lung maturation along with vigorous fluid replacement and tocolytic therapy (Thornton, 2011). Parenteral β-agonists are indisputably linked to pulmonary edema. Studies have also associated magnesium sulfate given for preeclampsia (Gandhi, 2014; Wilson, 2014; Xiao, 2014). Combined therapy is also causative. In one study of nearly 800 women given magnesium sulfate for preterm labor, 8 percent developed pulmonary edema, and half of this affected group had also received terbutaline (Samol, 2005).

TABLE 47-4

Some Causes and Associated Factors for Pulmonary Edema in Pregnancy

Noncardiogenic permeability edema: endothelial activation with capillary-alveolar leakage
Preeclampsia syndrome
Acute hemorrhage
Sepsis syndrome: pyelonephritis, metritis
Tocolytic therapy: β-mimetics, $MgSO_4$
Aspiration pneumonitis
Vigorous intravenous fluid therapy
Pancreatitis
Cardiogenic pulmonary edema: myocardial failure with hydrostatic edema from excessive pulmonary capillary pressure
Hypertensive cardiomyopathy
Obesity—adipositas cordis
Left-sided valvular disease
Vigorous intravenous fluid therapy
Pulmonary hypertension

Cardiogenic Hydrostatic Edema

Ventricular failure causing pulmonary edema in pregnancy is usually associated with some form of gestational hypertension. Although it can be due to congenital or acquired anatomical defects, diastolic dysfunction is frequently from chronic hypertension, obesity, or both (Jessup, 2003; Kenchaiah, 2002). In these women, acute systolic hypertension exacerbates diastolic dysfunction and causes pulmonary edema (Dennis, 2012; Gandhi, 2001). Of note, concentric and eccentric hypertrophy is two- to threefold more common in black women compared with white women (Drazner, 2005). In a case-control study of 28 gravidas with preeclampsia and pulmonary edema, half of them were undelivered (Gandhi, 2014).

In women with an underlying cardiomyopathy, heart failure is commonly precipitated by preeclampsia, hypertension, hemorrhage and anemia, and puerperal sepsis (Cunningham, 1986; Sibai, 1987). In many of these, when echocardiography is done later, systolic function is normal as measured by ejection fraction, but evidence for diastolic dysfunction can often be found (Aurigemma, 2004). The use of *brain natriuretic peptide (BNP)* has not been evaluated extensively in pregnancy (Seror, 2014). This neurohormone is secreted from ventricle myocytes and fibroblasts with distention seen in heart failure. In nonpregnant patients, values <100 pg/mL have an excellent negative-predictive value, and levels >500 pg/mL have an excellent positive-

predictive value. It is problematic that levels frequently are 100 to 500 pg/mL, and thus nondiagnostic (Ware, 2005). Values for N-terminal BNP and atrial natriuretic peptide (ANP) are both elevated with preeclampsia (Szabo, 2014; Tihtonen, 2007). This is discussed in greater detail in Chapter 4 (Renin, Angiotensin II, and Plasma Volume), and normal values for pregnancy are given in the Appendix (Serum and Blood Constituents).

Management

Acute pulmonary edema requires emergency care. Furosemide is given in 20- to 40-mg intravenous doses along with therapy to control severe hypertension. Further treatment depends on whether a woman is ante- or postpartum. A live fetus prohibits the use of cardioactive drugs that might rapidly lower peripheral resistance and in turn severely diminish uteroplacental circulation. The cause of cardiogenic failure is determined by echocardiography, which will help direct further therapy. Acute pulmonary edema is not, per se, an indication for emergency cesarean delivery.

ACUTE RESPIRATORY DISTRESS SYNDROME

Acute lung injury that causes a form of severe permeability pulmonary edema and respiratory failure is termed acute respiratory distress syndrome (ARDS). This is a pathophysiological continuum from mild pulmonary insufficiency to dependence on high inspired oxygen concentrations and mechanical ventilation. Uniform criteria for its diagnosis are lacking, and thus the incidence is variably reported for pregnancy. In one survey of the Nationwide Inpatient Sample, 2808 pregnant women with ARDS were identified (Rush, 2017). The incidence ranged from 36 to 60 cases per 100,000 births, and the maternal mortality rate was 9 percent. In its most extreme form, requiring ventilatory support, the associated mortality rate is 45 percent. This rate can be as high as 90 percent if caused or complicated by sepsis (Phua, 2009). Although gravidas are younger and usually healthier than the overall population, they still have mortality rates of 25 to 40 percent (Catanzarite, 2001; Cole, 2005). Finally, if ARDS develops antepartum, the perinatal mortality rate is correspondingly high.

Definitions

Most investigators define ARDS as radiographically documented pulmonary infiltrates, a ratio of arterial oxygen tension to the fraction of inspired oxygen (Pa_{O_2}:Fi_{O_2}) <200, and no evidence of heart failure (Mallampalli, 2010; Thompson, 2017). Revised by international consensus, the *Berlin Definition* was described by the ARDS Definition Task Force (2012) and includes categories of mild, moderate and severe. To date, for most interventional studies, a working diagnosis of *acute lung injury* is made when the Pa_{O_2}:Fi_{O_2} ratio is <300 and is coupled with dyspnea, tachypnea, oxygen desaturation, and radiographic pulmonary infiltrates (Wheeler, 2007).

Etiopathogenesis

ARDS is a pathophysiological description that begins with an acute lung injury from various causes (Table 47-5). In pregnant women, sepsis and diffuse infectious pneumonia are the two most common single-agent ARDS causes. Pyelonephritis, puerperal pelvic infection, and chorioamnionitis are the most frequent causes of sepsis. As discussed in Acute Pulmonary Edema, severe preeclampsia and obstetrical hemorrhage are also commonly associated with permeability edema. Importantly, more than half of pregnant women with ARDS have some combination of sepsis, hemorrhage, shock, and fluid overload. The contribution of *transfusion-related acute lung injury (TRALI)* is unclear (Chap. 41, Topical Hemostatic Agents).

TABLE 47-5

Some Causes of Acute Lung Injury and Respiratory Failure in Pregnant Women

Pneumonia: bacterial, viral, aspiration
Sepsis syndrome: chorioamnionitis, pyelonephritis, puerperal infection, septic abortion
Hemorrhage: shock, massive transfusion, transfusion-related acute lung injury (TRALI)
Preeclampsia syndrome
Tocolytic therapy
Embolism: amnionic fluid, trophoblastic disease, air, fat
Connective-tissue disease
Substance abuse
Irritant inhalation and burns
Pancreatitis
Drug overdose
Fetal surgery
Trauma
Sickle-cell disease
Miliary tuberculosis
Cerebral hemorrhage

Data from Cole, 2005; Duarte, 2014; Golombeck, 2006; Lapinsky, 2015; Martin, 2006; Sheffield, 2005; Sibai, 2014; Snyder, 2013; Zeeman, 2003, 2006.

Endothelial injury in the lung capillaries releases cytokines that recruit neutrophils to the inflammation site. Here, they elaborate more cytokines to worsen tissue injury. There are three stages of ARDS development. First, the *exudative phase* follows widespread injury to microvascular endothelium, including the pulmonary vasculature, and there is also alveolar epithelial injury. These result in increased pulmonary capillary permeability, surfactant loss or inactivation, diminished lung volume, and vascular shunting with resultant arterial hypoxemia. Next, the *fibroproliferative phase* usually begins 3 to 4 days later and lasts up to day 21. Last, the *fibrotic phase* results from healing, and despite this, the long-term prognosis for pulmonary function is surprisingly good (Herridge, 2003; Levy, 2015).

Clinical Course

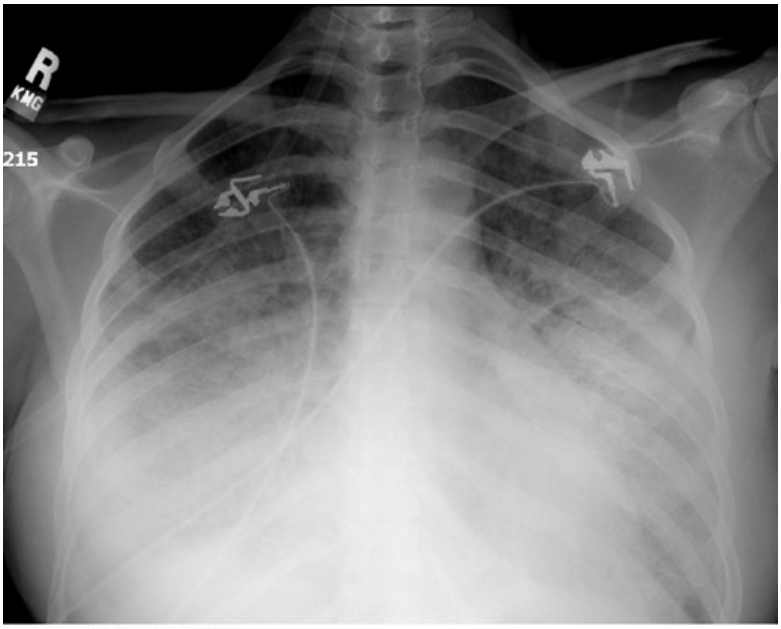
With pulmonary injury, the clinical condition depends largely on the insult magnitude, the ability to compensate for it, and the disease stage. For example, soon after the initial injury, physical findings are absent except perhaps hyperventilation. And at first, arterial oxygenation usually is adequate. Pregnancy-induced mild metabolic alkalosis may be accentuated by hyperventilation. With worsening, clinical and radiological evidence for pulmonary edema, decreased lung compliance, and increased intrapulmonary blood shunting become apparent. Progressive alveolar and interstitial

edema develop with extravasation of inflammatory cells and erythrocytes.

Ideally, pulmonary injury is identified at this early stage, and specific therapy is directed at the underlying insult. Further progression to acute respiratory failure is characterized by marked dyspnea, tachypnea, and hypoxemia. Additional lung volume loss results in worsening of pulmonary compliance and increased shunting. Diffuse abnormalities are heard by auscultation, and a chest radiograph characteristically demonstrates bilateral lung involvement (Fig. 47-1). At this phase, the injury ordinarily would be lethal in the absence of ventilatory support. When shunting exceeds 30 percent, severe refractory hypoxemia develops along with metabolic and respiratory acidosis that can result in myocardial irritability, dysfunction, and cardiac arrest.

FIGURE 47-1

Anteroposterior chest radiograph of a second-trimester pregnant woman with marked bilateral parenchymal and pleural opacification secondary to acute respiratory distress syndrome (ARDS) due to pyelonephritis.



Management

Reduced ARDS mortality rates have resulted from advances in care of the critically ill (Levy, 2015). This requires close attention to: (1) recognizing and treating underlying medical and surgical disorders, (2) minimizing procedures and their complications, (3) administering prophylaxis against venous thromboembolism, gastrointestinal bleeding, aspiration, and central venous catheter infection, (4) promptly diagnosing nosocomial infections, and (5) providing adequate nutrition.

In cases of severe acute lung injury, providing adequate oxygenation of peripheral tissues is balanced against maneuvers that further aggravate lung injury. At least intuitively, increasing oxygen delivery should produce a corresponding increase in tissue uptake, but this is difficult to measure. Support of systemic perfusion with intravenous crystalloid and blood is imperative. As discussed earlier, the trial conducted by the National Heart, Lung, and Blood Institute (2006) showed that pulmonary artery catheter use did not improve outcomes. Because sepsis is commonplace in lung injury, vigorous antimicrobial therapy is given for infection, and any necrotic tissues are debrided. Oxygen delivery can be greatly improved by correction of anemia. Specifically, each gram of hemoglobin carries 1.25 mL of oxygen when 90-percent saturated. By comparison, increasing the arterial P_{O_2} from 100 to 200 mm Hg results in the transport of only 0.1 mL of additional oxygen for each 100 mL of blood.

Reasonable goals in caring for the woman with severe lung injury are to attain a Pa_{O_2} of 60 mm Hg or 90-percent oxygen saturation using an inspired oxygen content <50 percent and positive end-expiratory pressures <15 mm Hg. With regard to the pregnancy, it remains controversial whether delivery of the fetus improves maternal oxygenation (Mallampalli, 2010). In a study of 29 women undergoing mechanical ventilation, 10 were delivered while

intubated (Lapinsky, 2015). This was associated with a modest improvement in respiratory function in perhaps half, but no factors were identified that predicted a better outcome.

Mechanical Ventilation

Noninvasive ventilation, that is, positive pressure ventilation by face mask, may be effective in some women in early stages of pulmonary insufficiency (Duarte, 2014). Early intubation is preferred in the gravida if respiratory failure is more likely than not, and especially if it appears imminent. Many successful formulas for mechanical ventilation are employed, and initially a tidal volume ≤6 mL/kg is optimal (Levy, 2015; Schwaiberger, 2016). High-frequency oscillation ventilation (HFOV) is controversial in ARDS (Ferguson, 2013; Slutsky, 2013). Adjustments are made to obtain a Pa_{O_2}>60 mm Hg or a hemoglobin oxygen saturation ≥90 percent and a Pa_{CO_2} of 35 to 45 mm Hg. Lower levels for Pa_{O_2} are avoided, because placental perfusion may be impaired (Levinson, 1974).

For women who require ventilation for any length of time, the maternal mortality rate is 10 to 20 percent. In a study of 51 such women, almost half had severe preeclampsia, and most required intubation postpartum. Eleven were delivered while being ventilated, and another six were discharged undelivered (Jenkins, 2003). There were two maternal deaths, including a woman who died as a complication of tocolytic treatment. In three other reports, maternal mortality rates ranged from 10 to 25 percent (Chen, 2003; Lapinsky, 2015; Schneider, 2003). In most cases, delivery did not improve maternal outcome.

Positive End-Expiratory Pressure

With severe lung injury and high intrapulmonary shunt fractions, it may not be possible to provide adequate oxygenation with usual ventilatory pressures, even with 100-percent oxygen. Positive end-expiratory pressure is usually successful in decreasing the shunt by recruiting collapsed alveoli. At low levels of 5 to 15 mm Hg, positive pressure can typically be used safely. At higher levels, impaired right-sided venous return can result in decreased cardiac output, lowered uteroplacental perfusion, alveolar overdistention, falling compliance, and barotrauma (Schwaiberger, 2016; Slutsky, 2013).

Extracorporeal Membrane Oxygenation

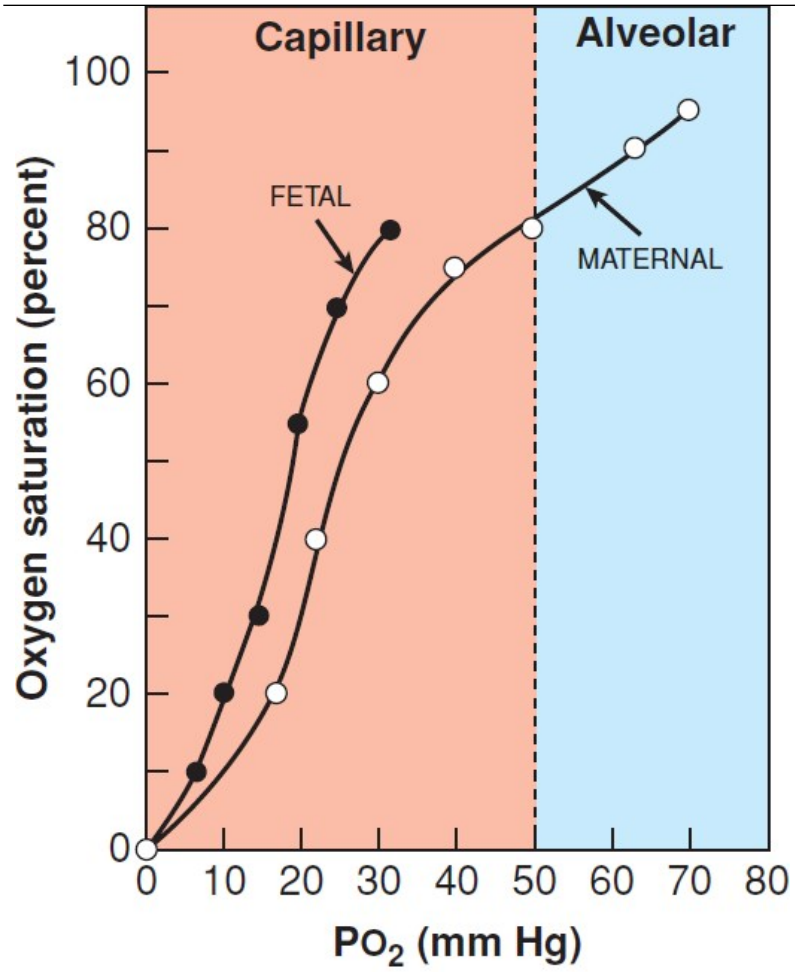
As discussed in Chapter 33 (Neonatal Encephalopathy and Cerebral Palsy), extracorporeal membrane oxygenation (ECMO) has been successfully used for neonatal meconium aspiration syndrome. Preliminary observation suggests that it may be useful in adults with ARDS (Brodie, 2011; Levy, 2015; Peek, 2009). ECMO use has been reported in pregnant women. In one study, 12 patients with influenza-induced lung failure were treated with ECMO, and of four maternal deaths, three were due to anticoagulation-related hemorrhage (Nair, 2011). In another study, the duration of support in four survivors was 2 to 28 days (Cunningham, 2006). In a review of 29 treated gravidas, 80 percent of cases were due to ARDS, and the maternal and perinatal mortality rate was 28 percent (Anselmi, 2015). Technical aspects of ECMO were reviewed by Brodie and Bacchetta (2011).

Fetal Oxygenation

The propensity of the hemoglobin molecule to release oxygen is described by the *oxyhemoglobin dissociation curve* (Fig. 47-2). For clinical purposes, the curve can be divided into an upper oxygen association curve representing the alveolar-capillary environment and a lower oxygen dissociation portion representing the tissue-capillary environment. Shifts of the curve have their greatest effect at the steep portion because they affect oxygen delivery. A rightward shift is associated with decreased hemoglobin affinity for oxygen and hence increased tissue-capillary oxygen interchange. Rightward shifts are produced by hypercapnia, metabolic acidosis, fever, and increased 2,3-diphosphoglycerate levels. During pregnancy, the erythrocyte concentration of 2,3-diphosphoglycerate is increased by approximately 30 percent. This favors oxygen delivery to both the fetus and maternal peripheral tissues.

FIGURE 47-2

Oxyhemoglobin dissociation curve. With higher oxygen tension (Pa_{O_2}) in the pulmonary alveoli, adult hemoglobin is maximally saturated compared with that at the lower oxygen tension in the tissue capillaries. Note that at any given oxygen tension, fetal hemoglobin carries more oxygen than adult hemoglobin, as indicated by percent saturation.



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Fetal hemoglobin has a higher oxygen affinity than adult hemoglobin. As seen in Figure 47-2, its curve is positioned to the left of the adult curve. To achieve 50-percent hemoglobin saturation, the Pao_2 must be 27 mm Hg in the mother compared with only 19 mm Hg in the fetus. Under normal physiological conditions, the fetus is constantly on the dissociation, or tissue, portion of the curve. Even with severe maternal lung disease and very low Pao_2 levels, oxygen displacement to fetal tissues is favored. Another example of this comes from pregnant women who live at high altitudes. Here, despite a maternal Pao_2 of only 60 mm Hg, the fetal Pao_2 is equivalent to that of fetuses at sea level (Subrevilla, 1971).

Intravenous Fluids

Although mortality outcomes are similar, conservative rather than liberal fluid management is associated with fewer days of mechanical ventilation (Wiedemann, 2006). Some pregnancy-induced physiological changes predispose to a greater risk of permeability edema from vigorous fluid therapy. Colloid oncotic pressure (COP) is determined by serum albumin concentration, and 1 g/dL exerts approximately 6 mm Hg pressure. As discussed in Chapter 4 (Gastrointestinal Tract), serum albumin concentrations normally drop in pregnancy. This results in a decline in oncotic pressure from 28 mm Hg in the nonpregnant woman to 23 mm Hg at term and to 17 mm Hg in the puerperium (Benedetti, 1979; Dennis, 2012). With preeclampsia, endothelial activation with leakage causes extravascular albumin loss and lowered serum albumin levels. As a result in these cases, oncotic pressure averages only 16 mm Hg antepartum and 14 mm Hg postpartum (Zinaman, 1985). These changes have a significant clinical effect on the *colloid oncotic pressure/wedge pressure gradient.* Normally, this gradient exceeds 8 mm Hg. However, when it is 4 mm Hg or less, the risk for pulmonary edema rises. No benefits are gained by albumin rather than crystalloid infusions in these women (Uhlig, 2014). These associations were reviewed by Dennis and Solnordal (2012).

Long-Term Outcomes

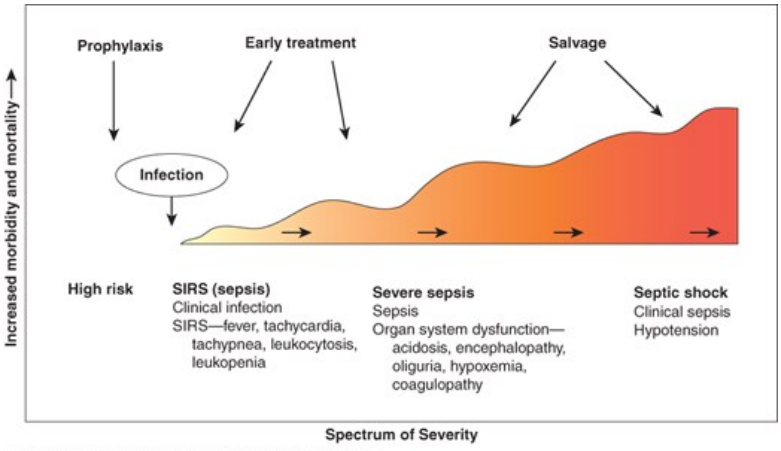
No long-term follow-up studies address gravidas who recover from ARDS. In nonpregnant subjects, risks for impaired global cognitive function at 3 and 12 months are significant (Pandharipande, 2013). Data from nonpregnant patients indicate a 1- to 2-year hiatus before basic normal activity is restored in all. In a 5-year follow-up study, Herridge and associates (2011) reported normal lung function but significant exercise limitation, physical and psychological sequelae, decreased physical quality of life, and increased use of health-care services.

SEPSIS SYNDROME

This syndrome is induced by a systemic inflammatory response to bacteria or viruses or their by-products such as endotoxins or exotoxins. The severity of the syndrome is a continuum or spectrum (Fig. 47-3). According to the Centers for Disease Control and Prevention (CDC), sepsis caused 6.2 percent of pregnancy-related deaths in the United States from 2011 to 2013 (Creanga, 2017). It was also a significant cause of maternal mortality in Michigan and the United Kingdom (Bauer, 2015; Mohamed-Ahmed, 2015; Nair, 2015).

FIGURE 47-3

The sepsis syndrome begins with a systemic inflammatory response syndrome (SIRS) in response to infection that may progress to septic shock.



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Infections that most commonly cause sepsis syndrome in obstetrics are pyelonephritis (Chap. 53, Cystitis and Urethritis), chorioamnionitis and puerperal sepsis (Chap. 37, Uterine Infection), septic abortion (Chap. 18, Inevitable Abortion), and necrotizing fasciitis (Chap. 37, Necrotizing Fasciitis). With severe sepsis, the mortality rate in nonpregnant patients is 20 to 35 percent and is 40 to 60 percent with septic shock (Angus, 2013; Munford, 2015). With shock, the mortality rate in pregnancy has been reported to be 30 percent (Mabie, 1997; Snyder, 2013). That said, the maternal mortality risk from sepsis is significantly underestimated (Bauer, 2015; Chebbo, 2016; Mohamed-Ahmed, 2015).

Etiopathogenesis

Most of what is known concerning sepsis pathogenesis comes from study of lipopolysaccharide—LPS or endotoxin (Munford, 2015). The lipid A moiety is bound by mononuclear blood cells, becomes internalized, and stimulates release of mediators and a series of complex downstream perturbations. Clinical aspects of the sepsis syndrome are manifest when cytokines are released that have endocrine, paracrine, and autocrine actions (Angus, 2013; Singer, 2016).

Although the sepsis syndrome in obstetrics may be caused by several pathogens, most cases represent a small group. For example, pyelonephritis complicating pregnancy caused by *Escherichia coli* and *Klebsiella* species commonly is associated with bacteremia and sepsis syndrome (Cunningham, 1987; Snyder, 2013). And although pelvic infections are usually polymicrobial, bacteria that cause severe sepsis syndrome are frequently endotoxin-producing Enterobacteriaceae, most commonly *E coli* (Eschenbach, 2015). Other pelvic pathogens are aerobic and anaerobic streptococci, *Bacteroides* species, and *Clostridium* species. Some strains of group A β-hemolytic streptococci and *Staphylococcus aureus*—including community-acquired methicillin-resistant strains (CA-MRSA)—produce a superantigen that activates T cells to rapidly cause all features of the sepsis syndrome—*toxic shock syndrome* (Moellering, 2011; Soper, 2011). This is discussed further in Chapter 37 (Breast Infections).

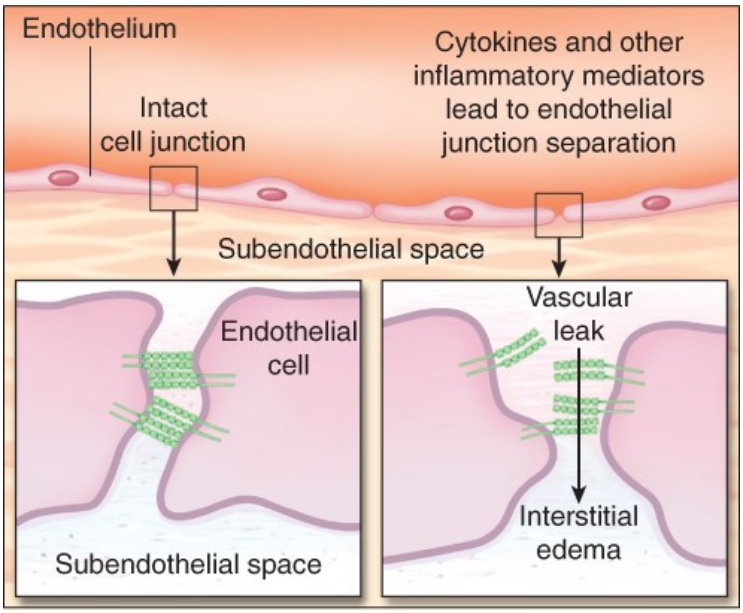
Potent bacterial *exotoxins* can also cause severe sepsis syndrome. Examples include exotoxins from *Clostridium perfringens* or *sordellii,* toxic-shock-syndrome toxin-1 (TSST-1) from *S aureus,* and toxic shock-like exotoxin from group A β-hemolytic streptococci (Daif, 2009; Soper, 2011). These last exotoxins cause rapid and extensive tissue necrosis and gangrene, especially of the postpartum uterus, and may cause profound cardiovascular collapse and maternal death (Nathan, 1993; Sugiyama, 2010). In a review discussed subsequently, the maternal mortality rate from these infections was 58 percent (Yamada, 2010).

Thus, the sepsis syndrome begins with an inflammatory response that is directed against microbial endotoxins and exotoxins (Angus, 2013). CD4 T cells and leukocytes are stimulated to produce proinflammatory compounds that include tumor necrosis factor-α (TNF-α), several interleukins, other cytokines, proteases, oxidants, and bradykinin that result in a "cytokine storm" (Russell, 2006). Many other cellular reactions then follow that include stimulation of pro- and antiinflammatory compounds, procoagulant activity, gene activation, receptor regulation, and immune suppression (Filbin, 2009; Moellering, 2011). It is also likely that interleukin-6 (IL-6) mediates myocardial suppression (Pathan, 2004).

The pathophysiological response to this cascade is selective vasodilation with maldistribution of blood flow. Leukocyte and platelet aggregation cause capillary plugging. Worsening endothelial injury causes profound permeability, capillary leakage, and interstitial fluid accumulation (Fig. 47-4). Depending on the degree of injury and inflammatory response, a pathophysiological and clinical continuum evolves as depicted in Figure 47-3. The clinical syndrome begins with subtle signs of sepsis from infection and terminates with *septic shock,* which is defined by hypotension unresponsive to intravenous hydration. In its early stages, clinical shock results primarily from decreased systemic vascular resistance that is not compensated fully by increased cardiac output. Hypoperfusion results in lactic acidosis, decreased tissue oxygen extraction, and end-organ dysfunction that includes acute lung and kidney injury.

FIGURE 47-4

Endothelial permeability. The normal interendothelial interface is shown in the left inset. Cytokines and other inflammatory mediators disassemble the cellular junctions, resulting in microvascular leaks (*right*).



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Clinical Manifestations

The sepsis syndrome has myriad clinical manifestations that, at least in part, are dependent on the specific invading microorganism and its particular endo- or exotoxins. Some of the general effects of LPS are as follows:

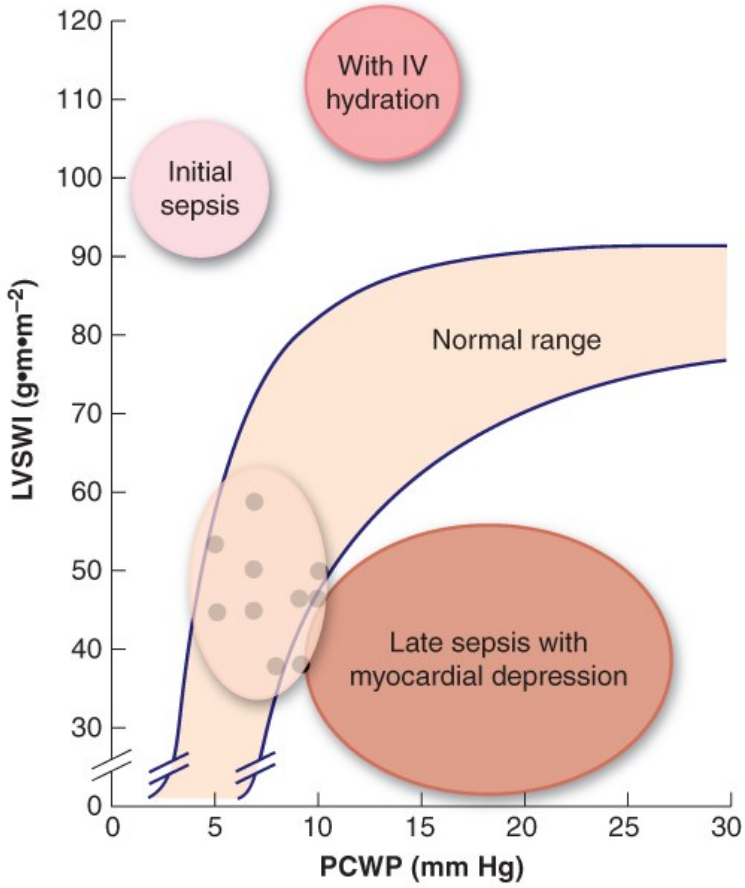
1. Central nervous system: confusion, delirium, somnolence, coma, combativeness, fever

2. Cardiovascular: tachycardia, hypotension
3. Pulmonary: tachypnea, arteriovenous shunting with dysoxia and hypoxemia, exudative infiltrates from endothelial-alveolar damage, pulmonary hypertension
4. Gastrointestinal: gastroenteritis—nausea, vomiting, and diarrhea; ileus; hepatocellular necrosis—jaundice, transaminitis
5. Renal: prerenal oliguria, azotemia, acute kidney injury, proteinuria
6. Hematological: leukocytosis or leukopenia, thrombocytopenia, activation of coagulation with disseminated intravascular coagulopathy
7. Endocrine: hyperglycemia, adrenal insufficiency
8. Cutaneous: acrocyanosis, erythroderma, bullae, digital gangrene.

Thus, although capillary leakage initially causes hypovolemia, if intravenous crystalloid is given at this point, then sepsis hemodynamically can be described as a high cardiac output, low systemic vascular resistance condition (Fig. 47-5). Concomitantly, pulmonary hypertension develops, and despite the high cardiac output, severe sepsis also causes myocardial depression (Munford, 2015; Ognibene, 1988). This is often referred to as the *warm phase* of septic shock. These findings are the most common cardiovascular manifestations of early sepsis, but they can be accompanied by some of the other clinical or laboratory aberrations listed above.

FIGURE 47-5

Hemodynamic effects of sepsis syndrome. Values for normal women at term are shown by dots. With early sepsis, there is high cardiac output and low vascular resistance. With fluid resuscitation, cardiac output increases even more, but so does capillary hydraulic pressure. With continued sepsis, there may be myocardial depression to further increase capillary hydraulic pressure. Decreased plasma oncotic pressure (serum albumin [g] × 6 mm Hg) contributes to interstitial lung fluid and endo/epithelial leak causes alveolar flooding. LVSWI = left ventricular stroke work index; PCWP = pulmonary capillary wedge pressure.



The response to initial intravenous hydration may be prognostic. Most pregnant women who have early sepsis show a salutary response with crystalloid and antimicrobial therapy, and if indicated, debridement of infected tissue. Conversely, if hypotension is not corrected following vigorous fluid infusion, then the prognosis is more guarded. At this juncture, if there also is no response to β-adrenergic inotropic agents, this indicates severe and unresponsive extracellular fluid extravasation with vascular insufficiency, overwhelming myocardial depression, or both. Oliguria and continued peripheral vasoconstriction characterize a secondary, *cold phase* of septic shock that is rarely survived. Another poor prognostic sign is continued renal, pulmonary, and cerebral dysfunction once hypotension has been corrected (Angus, 2013; Chebbo, 2016). The average risk of death increases by 15 to 20 percent with failure of each organ system. With three systems, mortality rates are 70 percent (Martin, 2003; Wheeler, 1999).

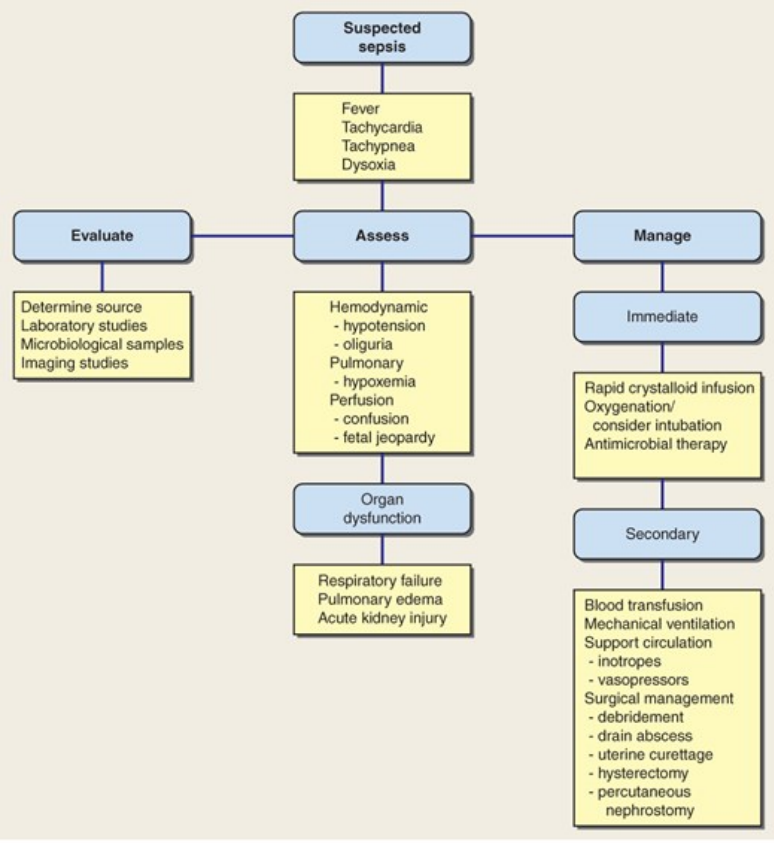
Management

In 2004, an international consensus effort was launched as the *Surviving Sepsis Campaign* (Dellinger, 2013). The cornerstone of management is *early goal-directed management,* and it stresses prompt recognition of serious bacterial infection and close monitoring of vital signs and urine flow. It remains controversial if institution of this protocol has improved survival rates (ARISE Investigators, 2014; Mouncey, 2015; ProCESS Investigators, 2014). Similar conclusions were reached with sets of early warning systems in obstetrics (Edwards, 2015; Mhyre, 2014). Albright and associates (2017) have validated the Sepsis in Obstetrics Score to identify the risk of ICU admission for sepsis.

An algorithm for management of sepsis syndrome is shown in Figure 47-6. The three basic steps are performed as simultaneously as possible and include evaluation of the sepsis source and its sequelae, cardiopulmonary function assessment, and immediate management. The most important step in sepsis management is rapid infusion of 2 L and sometimes as many as 4 to 6 L of crystalloid fluids to restore renal perfusion in severely affected women (Vincent, 2013). Simultaneously, appropriately chosen broad-spectrum antimicrobials are begun. Because hemoconcentration is caused by the capillary leak, if anemia coexists, then blood is given. Maintaining the hemoglobin concentration at ≥9 g/dL did not have superior outcomes compared with that of ≥7 g/dL (Holst, 2014). That said, fetal oxygenation is improved by the higher concentration.

FIGURE 47-6

Algorithm for evaluation and management of sepsis syndrome. Rapid and aggressive implementation is paramount for success. The three steps—Evaluate, Assess, and Manage—are carried out as simultaneously as possible.



The use of colloid solution such as hetastarch is controversial (Angus, 2013; Ware, 2000). One randomized trial comparing hydroxyethyl starch and Ringer acetate reported a higher mortality rate with the starch solution (Perner, 2012). Another study found equivalent results with 6-percent hydroxyethyl starch compared with normal saline (Myburgh, 2012). Albumin was not found to be superior to crystalloids (Caironi, 2014).

Aggressive volume replacement ideally is promptly followed by urinary output of at least 30 and preferably 50 mL/hr, as well as other indicators of improved perfusion. If not, then consideration is given for vasoactive drug therapy (Pacheco, 2014). Mortality rates are high when sepsis is further complicated by respiratory or renal failure. With severe sepsis, damage to pulmonary capillary endothelium and alveolar epithelium causes alveolar flooding and pulmonary edema. This may occur even with low or normal pulmonary capillary wedge pressures, as with the ARDS discussed in Acute Respiratory Distress Syndrome and depicted in Figure 47-1.

Broad-spectrum antimicrobials are chosen empirically based on the probable source of infection. They are given promptly in maximal doses after appropriate cultures are taken of blood, urine, or exudates not contaminated by normal flora. In severe sepsis, appropriate empirical coverage results in better survival rates (Barochia, 2010; MacArthur, 2004). In obstetrics acute pyelonephritis is usually caused by Enterobacteriaceae, as discussed in Chapter 53 (Cystitis and Urethritis). For pelvic infections, empirical coverage with regimens such as ampicillin plus gentamicin plus clindamycin generally suffices (Chap. 37, Pathogenesis and Clinical Course). Associated incisional and other soft-tissue infections are increasingly likely to be caused by methicillin-resistant *S aureus*, thus vancomycin therapy may be added (Klevens, 2007; Rotas, 2007). With a septic abortion, a Gram-stained smear may be helpful in identifying *Clostridium* species or group A streptococcal organisms. This is also true for deep fascial infections.

Surgical Treatment

Continuing sepsis may prove fatal, and debridement of necrotic tissue or drainage of purulent material is crucial (Nelson, 2015; Pacheco, 2014). In

obstetrics, the major causes of sepsis are infected abortion, pyelonephritis, and puerperal pelvic infections, which include metritis and infections of perineal lacerations or of hysterotomy or laparotomy incisions. With a septic abortion, uterine contents must be removed promptly by curettage as described in Chapter 18 (Inevitable Abortion). Hysterectomy is seldom indicated unless gangrene has resulted.

For women with pyelonephritis, continuing sepsis should prompt a search for obstruction caused by calculi or by a perinephric or intrarenal phlegmon or abscess. Renal sonography or "one-shot" pyelography can help diagnose obstruction and calculi. With obstruction, ureteral catheterization, percutaneous nephrostomy, or flank exploration may be lifesaving (Chap. 53, Reflux Nephropathy). Computed tomography (CT) or magnetic-resonance imaging aids in identifying a phlegmon or abscess.

Puerperal Infections

Most cases of puerperal pelvic sepsis are clinically manifested in the first several days postpartum, and intravenous antimicrobial therapy without tissue debridement is generally curative. There are at least three exceptions.

First, massive uterine myonecrosis can be caused by group A β-hemolytic streptococcal or clostridial infections (Soper, 2011; Sugiyama, 2010; Yamada, 2010). Those with early-onset disease present with findings listed in Table 47-6. The mortality rate in these women with gangrene as shown in Figure 47-7 is high, and prompt hysterectomy may be lifesaving (Mabie, 1997; Nathan, 1993). Group A β-hemolytic streptococci and clostridial colonization or infection also cause toxic-shock syndrome without obvious gangrene (Mason, 2012). These are due to either streptococcal toxic-shock-syndrome-like toxin or clostridial exotoxin that evolved from *S aureus* (Chap. 37, Breast Infections). In many of these cases, there is bacteremia and widespread tissue invasion, but with an intact uterus and abdominal incision. If uterine necrosis can be excluded—usually by CT scanning—then in our experiences, as well as in others, hysterectomy may not be necessary (Soper, 2011). Still, these infections are highly lethal (Yamada, 2010).

TABLE 47-6

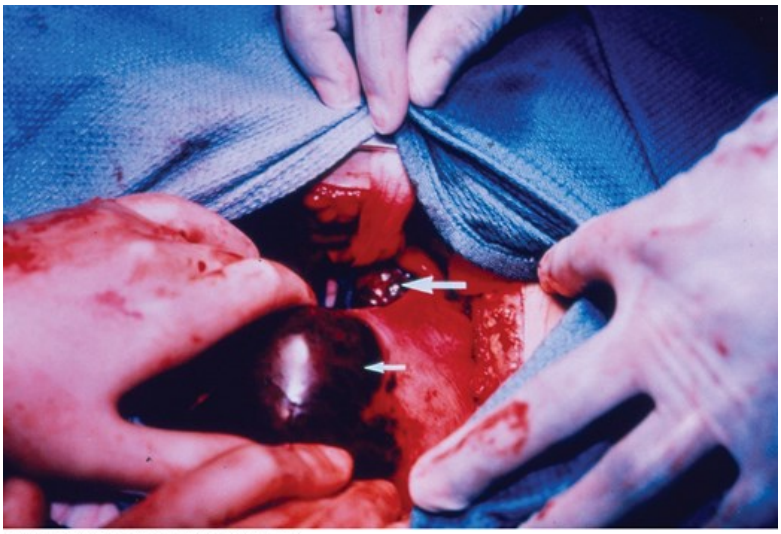
Clinical Findings in 55 Women with Group A β-Hemolytic Infection Manifest within 12 Hours of Delivery

Finding	Frequency (%)
Multiparous	83
Third-trimester	90
Flulike symptoms	
High fever	94
Upper respiratory	40
Gastrointestinal	49
Uterine hypertonus	73
Early-onset shock	91
Mortality	
Maternal	58
Perinatal	66

Data from Yamada, 2010.

FIGURE 47-7

A fatal case of group A β-hemolytic *Streptococcus pyogenes* puerperal infection following an uncomplicated vaginal delivery at term. The infection caused uterine gangrene and overwhelming sepsis syndrome. Arrows point to overtly "ballooned-out" black gangrenous areas of the postpartum uterus at the time of laparotomy for hysterectomy.



As a second exception, necrotizing fasciitis of the episiotomy site or of the abdominal surgical incision is a surgical emergency. As described by Gallup and coworkers (2002), these infections are aggressively managed as discussed in Chapter 37 (Necrotizing Fasciitis). Sinha and colleagues (2015) described a woman with *Fournier gangrene* who required radical debridement and colostomy.

As a final exception, persistent or aggressive postpartum uterine infection with necrosis, uterine incision dehiscence, and severe peritonitis may lead to sepsis (Chap. 37, Parametrial Phlegmon). In this regard, women following cesarean delivery who are suspected of having peritonitis should be carefully evaluated for uterine incisional necrosis or bowel perforation. These infections tend to be less aggressive than necrotizing group A streptococcal infections and develop later postpartum. CT imaging of the abdomen and pelvis can frequently disclose these. If either is suspected, then prompt surgical exploration is indicated. With incisional necrosis, hysterectomy is usually necessary (Fig. 37-5). Finally, peritonitis and sepsis much less commonly may result from a ruptured parametrial, intraabdominal, or ovarian abscess (Chap. 37, Necrotizing Fasciitis).

Adjunctive Therapy

As shown in Figure 47-6, a woman with severe sepsis syndrome is supported with continuing crystalloid infusion, blood transfusions, and ventilation. In some cases, other measures may be necessary. Vasoactive drugs are not given unless aggressive fluid treatment fails to correct hypotension and perfusion abnormalities. First-line vasopressors are norepinephrine, epinephrine, dopamine, dobutamine, or phenylephrine (Vincent, 2013).

The use of corticosteroids remains controversial. Some studies, but not all, show a salutary effect of corticosteroid administration. It is thought that *critical illness-related corticosteroid insufficiency—CIRCI*—may play a role in recalcitrant hypotension. Thus, corticosteroids may be considered for use in vasopressor-dependent patients (Angus, 2013; Munford, 2015).

Endotoxin stimulates endothelial cells to upregulate tissue factor and thus procoagulant production (Cunningham, 2015). Consumptive coagulopathy associated with sepsis is discussed in Chapter 41 (Obstetrical Coagulopathies). At the same time, it decreases the anticoagulant action of activated protein C. Several agents developed to block coagulation, however, did not improve outcomes. Some include *recombinant activated protein C*, *antithrombin III, platelet-activating factor antagonist,* and *tissue factor pathway inhibitor* (Munford, 2015; Wenzel, 2012).

TRAUMA

Depending on definitions used, 10 to 20 percent of gravidas suffer physical trauma (Jain, 2015; Lucia, 2016). Moreover, injury-related deaths are the

most commonly identified nonobstetrical cause of maternal mortality (Brown, 2013a; Horon, 2001). In a California study of 4.8 million pregnancies, almost 1 in 350 women were hospitalized for injuries from assaults (El Kady, 2005). From Parkland Hospital, motor vehicle accidents and falls accounted for 85 percent of injuries sustained by 1682 pregnant women (Hawkins, 2007). From the National Violent Death Reporting System, Palladino and colleagues (2011) found 2.0 pregnancy-associated suicides per 100,000 live births. The rate was 2.9 per 100,000 for pregnancy-associated homicides. Notably, intimate-partner violence may be linked to these suicides (Martin, 2007). Finally, injury prevention and education of high-risk patients may help to decrease morbidity (Chisolm, 2017; Lucia, 2016).

Physical Abuse

According to the CDC, intimate-partner violence describes physical, sexual, or psychological harm by a current or former partner or spouse (Breiding, 2015). Such violence affects 1 in 5 women each year. One goal in violence prevention for *Healthy People 2010* was the reduction of physical abuse directed at women by male partners. The Pregnancy Risk Assessment Monitoring Systems (PRAMS) report showed some improvement in these areas (Suellentrop, 2006).

Even more appalling is that physical violence directed at women continues during pregnancy. Abuse is linked to poverty, poor education, and use of tobacco, alcohol, and illicit drugs (Centers for Disease Control and Prevention, 2008). Unfortunately, abused women tend to remain with their abusers, and the major risk factor for intimate-partner homicide is prior domestic violence (Campbell, 2007). Finally, women seeking pregnancy termination have a higher incidence of intimate-partner violence (Bourassa, 2007).

The woman who is physically abused tends to present late, if at all, for prenatal care. In one study, pregnant women hospitalized in California as a result of assault had significantly increased perinatal morbidity rates (El Kady, 2005). Immediate sequelae included uterine rupture, preterm delivery, and maternal and perinatal death. Subsequent outcomes included increased rates of placental abruption, preterm and low-birthweight newborns, and other adverse outcomes. Silverman and associates (2006) reported similar results from PRAMS, which included more than 118,000 pregnancies in 26 states.

Preventatively, the American College of Obstetricians and Gynecologists (2012) recommend universal screening for intimate-partner violence at the initial prenatal visit, during each trimester, and again at the postpartum visit (Chap. 9, Alcohol). Others recommend a case-finding approach based on clinical suspicion (Robertson-Blackmore, 2013).

Sexual Assault

According to the National Intimate Partner and Sexual Violence Survey (Black, 2014), an estimated 1.2 million women will be sexually assaulted each year. Satin and coworkers (1992) reviewed more than 5700 female sexual assault victims in Dallas County and reported that 2 percent were pregnant. Associated physical trauma is common (Sugar, 2004). From a forensic standpoint, the evidence collection protocol is not altered (Linden, 2011).

In addition to attention to physical injuries, exposure to sexually transmitted diseases must be considered. The CDC (2015) recommends antimicrobial prophylaxis against gonorrhea, chlamydial infection, bacterial vaginosis, and trichomoniasis (Table 47-7). If the woman is not pregnant, another very important aspect is emergency contraception, as recommended by the American College of Obstetricians and Gynecologists (2016; 2017a) and discussed in Chapter 38 (Emergency Contraception).

TABLE 47-7

Guidelines for Prophylaxis against Sexually Transmitted Disease in Pregnant Victims of Sexual Assault

Prophylaxis Against	Regimen	Alternative
Neisseria gonorrhoeae	Ceftriaxone 250 mg IM single dose ***plus*** Azithromycin 1 g orally single dose	Cefixime 400 mg orally single dose ***plus*** Azithromycin 1 g orally single dose
Chlamydia trachomatis	Azithromycin 1 g orally single dose[a] ***or*** Amoxicillin 500 mg orally three times daily for 7 days	Erythromycin-base 500 mg orally four times daily for 7 days ***or*** Levofloxacin 500 mg orally once daily for 7 days[b] ***or*** Ofloxacin 300 mg orally twice daily for 7 days[b]
Bacterial vaginosis	Metronidazole 500 mg orally twice daily for 7 days ***or*** Metronidazole gel 0.75%, one full applicator (5 g) intravaginally once daily for 5 days ***or*** Clindamycin cream 2%, one full applicator (5 g) intravaginally at bedtime for 7 days	Tinidazole 2 g orally once daily for 2 days[b] ***or*** Tinidazole 1 g orally daily for 5 days ***or*** Clindamycin 300 mg orally twice daily for 7 days ***or*** Clindamycin ovules 100 mg intravaginally at bedtime for 3 days
Trichomonas vaginalis	Metronidazole 2 g orally single dose ***or*** Tinidazole 2 g orally single dose[b]	Metronidazole 500 mg orally twice daily for 7 days
Hepatitis B (HBV)	If not previously vaccinated, give first dose HBV vaccine, repeat at 1–2 and 4–6 months	
HIV	Consider retroviral prophylaxis if risk for HIV exposure is high	

[a]For nonpregnant women, doxycycline, 100 mg orally twice daily for 7 days, can be given instead.

[b]Pregnancy category C.

HIV = human immunodeficiency virus; IM = intramuscularly.

Data from Centers for Disease Control and Prevention, 2015.

Finally, the importance of psychological counseling for the rape victim and her family cannot be overemphasized. A 30- to 35-percent lifetime risk each for posttraumatic stress disorder, major depression, and suicide contemplation follows sexual assault (Linden, 2011).

Automobile Accidents

At least 3 percent of pregnant women are involved in motor vehicle accidents each year in the United States. Using data from PRAMS, Sirin and colleagues (2007) estimated that 92,500 gravidas are injured annually. Motor-vehicle crashes are the most common causes of serious, life-threatening,

or fatal blunt trauma during pregnancy (Brown, 2013a; Mendez-Figueroa, 2013, 2016; Vladutiu, 2013). Mattox and Goetzl (2005) report these accidents to be the leading cause of traumatic fetal deaths as well. This was also true from our experiences from Parkland Hospital (Hawkins, 2007). Traffic crashes are most frequent in the second trimester (Redelmeier, 2014). As with all motor vehicle crashes, alcohol use is often associated. But sadly, as many as half of accidents occur without seat-belt use, and many of these deaths would likely be preventable by the three-point restraints shown in Figure 47-8 (Luley, 2013; Schuster, 2016). Seat belts prevent contact with the steering wheel, and they reduce abdominal impact pressure (Motozawa, 2010).

FIGURE 47-8

Illustration showing correct use of three-point automobile restraint. The upper belt is *above* the uterus, and the lower belt fits snugly across the upper thighs and well *below* the uterus.

Original concerns regarding injuries caused by airbag deployment have been somewhat allayed (Luley, 2013; Matsushita, 2014). One study included 30 such women from 20 to 37 weeks' gestation whose airbag deployed in accidents with a median speed of 35 mph (Metz, 2006). A third did not use seat belts, and there was one fetal death from the single case of placental abruption. In a retrospective cohort study that included 2207 pregnant women in crashes with airbag deployment, perinatal outcomes were not clinically different from 1141 controls without airbags (Schiff, 2010). Importantly, 96 percent of both groups used seat belts. Thus, it appears that injuries with airbag deployment are related to the severity of the crash (Mendez-Figueroa, 2016).

Other Blunt Trauma

Some other common causes of blunt trauma are falls and aggravated assaults. In the California review reported by El Kady and associates (2005), intentionally inflicted injuries were present in approximately a third of pregnant women who were hospitalized for trauma. Less common are blast or crush injury (Sela, 2008). With blunt trauma, intraabdominal injuries can be serious. Even so, bowel injuries are less frequent because of the protective effect of a large uterus. Still, diaphragmatic, splenic, liver, and kidney damage may also be sustained. Particularly worrisome is the specter of amnionic-fluid embolism, which has been reported with even mild trauma (Ellingsen, 2007; Pluymakers, 2007). Retroperitoneal hemorrhage is possibly more common than in nonpregnant women (Takehana, 2011).

Orthopedic injuries are also encountered with some regularity (Desai, 2007). From the Parkland Hospital trauma unit, 6 percent of 1682 pregnant women evaluated had orthopedic injuries. This subset was also at increased risk for placental abruption, preterm delivery, and perinatal mortality. In a review of 101 pelvic fractures during pregnancy, there was a 9-percent maternal and 35-percent fetal mortality rate (Leggon, 2002). In another study of pelvic and acetabular fractures during 15 pregnancies, there was one maternal death, and four of 16 fetuses died (Almog, 2007). Finally, head trauma and neurosurgical care raise unique issues (Qaiser, 2007).

Fetal Injury and Death

Perinatal death rates increase with the severity of maternal injuries. Fetal death is more likely with direct fetoplacental injury, maternal shock, pelvic fracture, maternal head injury, or hypoxia (Ikossi, 2005; Pearlman, 2008). Motor vehicle accidents caused 82 percent of fetal deaths from trauma. Death was caused by placental injury in half and by uterine rupture in 4 percent (Weiss, 2001).

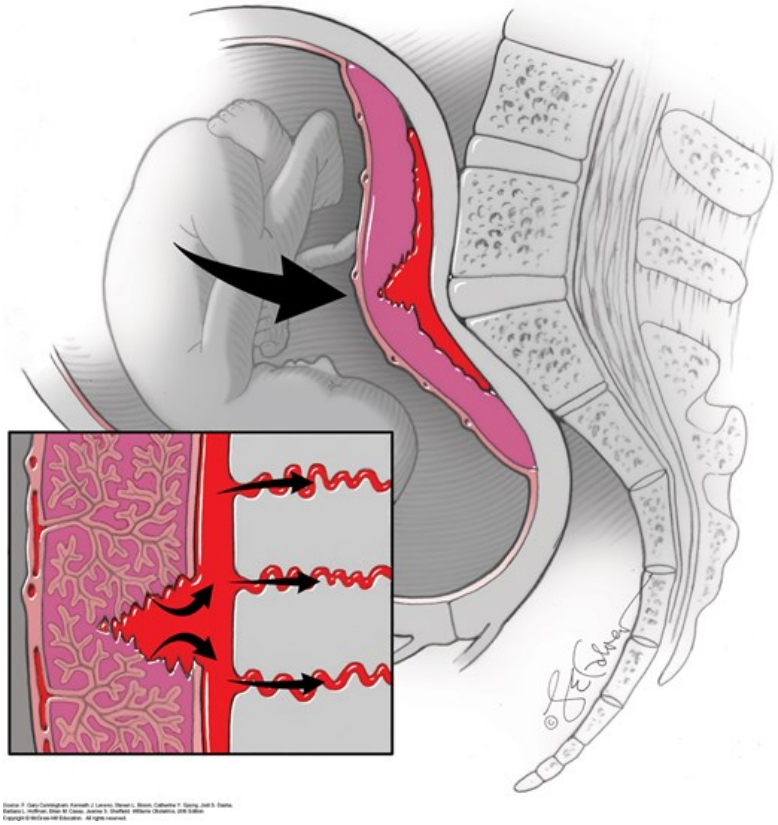
Although uncommon, fetal skull and brain injuries are more likely if the head is engaged and the maternal pelvis is fractured (Palmer, 1994). Conversely, fetal head injuries, presumably from a contrecoup effect, may be sustained in unengaged vertex or nonvertex presentations. Fetal skull fractures are rare and best seen using CT imaging (Sadro, 2012). One example is Figure 46-4. Other sequelae include intracranial hemorrhage (Gherman, 2014; Green-Thompson, 2005). A newborn with paraplegia and contractures associated with a motor vehicle accident sustained several months before birth was described by Weyerts and colleagues (1992). Other injuries have included fetal decapitation or incomplete midabdominal fetal transection at midpregnancy (Rowe, 1996; Weir, 2008).

Placental Injuries

Catastrophic events that occur with blunt trauma include placental injuries—abruption or placental tears (Fig. 47-9). Placental separation from trauma is likely caused by deformation of the elastic myometrium around the relatively inelastic placenta (Crosby, 1968). This may result from a deceleration injury as the large uterus meets the immovable steering wheel or seat belt. Some degree of abruption complicates 1 to 6 percent of minor injuries and up to 50 percent of major injuries (Pearlman, 1990; Schiff, 2002). Abruption was found to be more likely if vehicle speed exceeded 30 mph (Reis, 2000).

FIGURE 47-9

Mechanism of placental tear or "fracture" caused by a deformation-reformation injury. Placental abruption is seen as blood collecting in the retroplacental space. **Inset**. From here, blood can be forced into placental bed venules and enter maternal circulation. Such fetomaternal hemorrhage may be identified with Kleihauer-Betke testing.

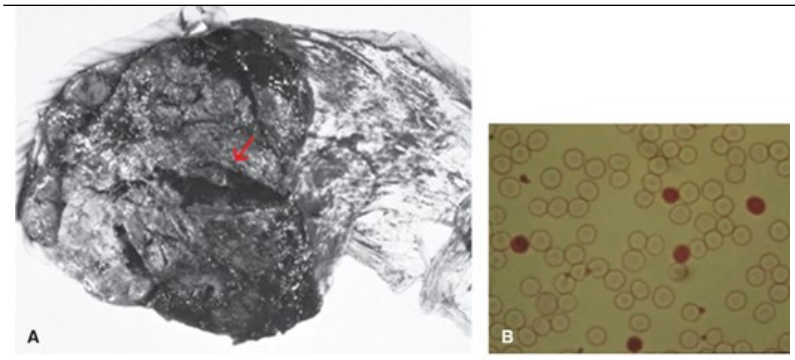


Clinical findings with traumatic abruption may be similar to those for spontaneous placental abruption (Chap. 41, Frequency). Kettel and coworkers (1988) emphasized that traumatic abruption may be occult and unaccompanied by uterine pain, tenderness, or bleeding. In our experiences with 13 such women at Parkland Hospital, 11 had uterine tenderness, but only five had vaginal bleeding. Because traumatic abruption is more likely to be concealed and generate higher intrauterine pressures, associated coagulopathy is more likely than with nontraumatic abruption (Cunningham, 2015). Partial separation may also generate uterine activity, which is described more fully in Thermal Injury. Other features are evidence of fetal compromise such as fetal tachycardia, sinusoidal pattern, late decelerations, acidosis, and fetal death.

If the abdominal force associated with trauma is considerable, then the placenta can be torn or "fractured" (see Fig. 47-9). If so, then life-threatening fetal hemorrhage may be encountered either into the amnionic sac or by fetomaternal hemorrhage (Pritchard, 1991). The tear is linear or stellate and is caused by rapid deformation and reformation (Fig. 47-10). Especially if there is ABO compatibility, fetomaternal hemorrhage is quantified using a Kleihauer-Betke stain of maternal blood. A small amount of fetal-maternal bleeding has been described in up to a third of trauma cases, and in 90 percent of these, the volume is <15 mL (Goodwin, 1990; Pearlman, 1990). Parenthetically, nontraumatic placental abruption is much less often associated with significant fetomaternal hemorrhage because only minimal fetal blood enters into the intervillous space. With traumatic abruption, however, massive fetomaternal hemorrhage may follow. In one study, the risk of associated uterine contractions and preterm labor was a 20-fold if there was evidence for a fetomaternal bleed (Muench, 2004). With severe fetal bleeding, long-term adverse neurological outcomes are frequent (Kadooka, 2014).

FIGURE 47-10

A. Partial placental abruption in which the adherent blood clot has been removed. Note the laceration of the placenta (*arrow*), which caused fetal death from massive fetomaternal hemorrhage. **B.** Kleihauer–Betke stain of a peripheral smear of maternal blood. The dark cells that constituted 4.5 percent of red blood cells are fetal in origin, whereas the empty cells are maternal.



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Uterine Rupture

Blunt trauma leads to uterine rupture in <1 percent of severe cases (American College of Obstetricians and Gynecologists, 2017b). Rupture is more likely in a previously scarred uterus and is usually associated with a direct impact of substantial force. Decelerative forces following a 25-mph collision can generate up to 500 mm Hg of intrauterine pressure in a properly restrained woman (Crosby, 1968). Clinical findings may be identical to those for placental abruption with an intact uterus, and maternal and fetal deterioration are soon inevitable. Pearlman and Cunningham (1996) described uterine fundal "blowout" with fetal decapitation in a 20-week pregnancy following a high-speed collision. Similarly, Weir and colleagues (2008) described supracervical uterine avulsion and fetal transection at 22 weeks. CT scanning may be useful to diagnose uterine rupture with a dead fetus or placental separation (Kopelman, 2013; Manriquez, 2010; Sadro, 2012).

Penetrating Trauma

In a study of 321 pregnant women with abdominal trauma, Petrone (2011) reported a 9-percent incidence of penetrating injuries. Of these, 77 percent were gunshot wounds and 23 percent were stab wounds. The incidence of maternal visceral injury with penetrating trauma is only 15 to 40 percent compared with 80 to 90 percent in nonpregnant individuals (Stone, 1999). When the uterus sustains penetrating wounds, the fetus is more likely than the mother to be seriously injured. Indeed, although the fetus sustains injury in two thirds of cases with penetrating uterine injuries, maternal visceral injuries are seen in only 20 percent. Still, their seriousness is underscored in that maternal-fetal mortality rates are significantly higher than those seen with blunt abdominal injuries in pregnancy. Specifically, maternal mortality rates were 7 versus 2 percent, and fetal mortality rates were 73 versus 10 percent, respectively.

Management of Trauma

Maternal and fetal outcomes are directly related to the severity of injury. That said, commonly used methods of severity scoring do not take into account significant morbidity and mortality rates related to placental abruption and thus to pregnancy outcomes. In a study of 582 pregnant women hospitalized for injuries, the injury severity score did not accurately predict adverse pregnancy outcomes (Schiff, 2005). Importantly, relatively minor injuries were associated with preterm labor and placental abruption. Others have reached similar conclusions (Biester, 1997; Ikossi, 2005). In a study of 317 women at 24 weeks' gestation or more who had "minor trauma," 14 percent had clinically significant uterine contractions requiring extended fetal evaluation past 4 hours (Cahill, 2008).

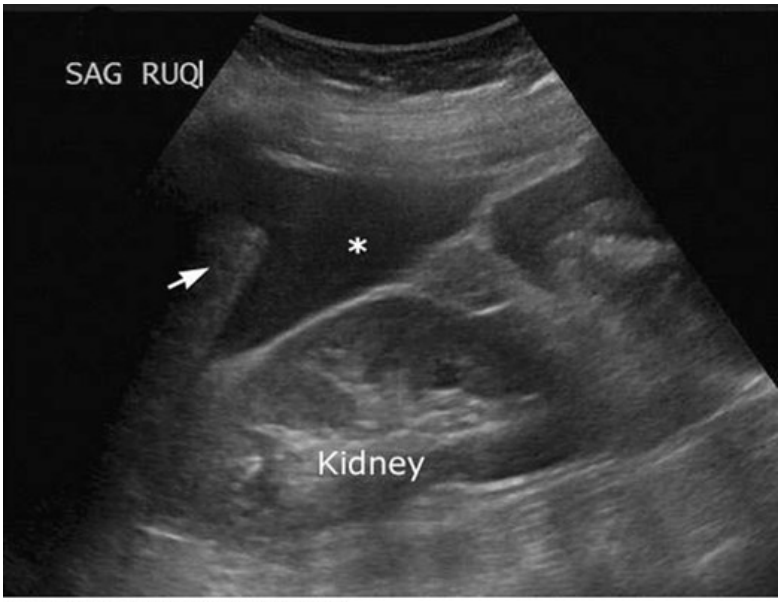
With few exceptions, treatment priorities in injured pregnant women are multidisciplinary (Barraco, 2010; Mendez-Figueroa, 2016). Primary goals are evaluation and stabilization of maternal injuries. Attention to fetal assessment during the acute evaluation may divert attention from life-threatening maternal injuries (American College of Obstetricians and Gynecologists, 2017b; Brown, 2009). Basic rules of resuscitation include ventilation, arrest of hemorrhage, and treatment of hypovolemia with crystalloid and blood products. After midpregnancy, the large uterus is positioned off the great vessels to diminish its effect on vessel compression and cardiac output (Nelson, 2015).

Following emergency resuscitation, evaluation is continued for fractures, internal injuries, bleeding sites, and placental, uterine, and fetal trauma. Radiography is not proscribed, but special attention is given each indication. Not surprisingly, one report observed that pregnant trauma victims had less radiation exposure than nonpregnant controls (Ylagan, 2008). Some advocate screening abdominal sonography followed by CT scanning for positive sonographic findings (Brown, 2005; Saphier, 2014). Procedures used include the *FAST scan—focused assessment with sonography for*

trauma. This examination is a 5-minute, four- to six-view imaging study that evaluates perihepatic, perisplenic, pelvic, and pericardial views (Mendez-Figueroa, 2016). In general, if fluid is seen in any of these views, then the volume is >500 mL (Fig. 47-11). Importantly, this amount has not been corroborated for pregnancy. In some cases, open peritoneal lavage may be informative (Tsuei, 2006).

FIGURE 47-11

Fast scan. Upper quadrant scan shows anechoic free fluid (asterisk) between the liver edge (arrow) and kidney (Morison pouch). The patient had 2500 mL of blood in the peritoneal cavity. (From Mendez-Figueroa H, Rouse DJ: Trauma in pregnancy. In Yeomans ER, Hoffman BL, Gilstrap LC III, et al (eds): Cunningham and Gilstrap's Operative Obstetrics 3rd ed, New York McGraw-Hill Education, 2016, In press.)



Penetrating injuries in most cases must be evaluated using radiography. Because clinical response to peritoneal irritation is blunted during pregnancy, an aggressive approach to exploratory laparotomy is pursued. Whereas exploration is mandatory for abdominal gunshot wounds, some clinicians advocate close observation for selected stab wounds. Diagnostic laparoscopy has also been used (Chap. 46, Medications and Surgeries).

Cesarean Delivery

The necessity for cesarean delivery depends on several factors. Laparotomy itself is not an indication for hysterotomy. Some considerations include gestational age, fetal condition, extent of uterine injury, and whether the large uterus hinders adequate management of other intraabdominal injuries (Tsuei, 2006).

Electronic Monitoring

Because fetal well-being may reflect the status of the mother, fetal monitoring is another "vital sign" that helps evaluate the extent of maternal injuries. Even if the mother is stable, electronic monitoring may suggest placental abruption. In a study by Pearlman and coworkers (1990), no woman had an abruption if uterine contractions were less often than every 10 minutes within the 4 hours after trauma was sustained. Almost 20 percent of women who had contractions more frequently than every 10 minutes in the first 4 hours had an associated placental abruption. In these cases, abnormal tracings were common and included fetal tachycardia and late decelerations. Conversely, no adverse outcomes were reported in women who had normal monitor tracings (Connolly, 1997). Importantly, if tocolytics are used for these contractions, they may obfuscate findings, and we do not recommend them.

Because placental abruption usually develops early following trauma, fetal monitoring is begun as soon as the mother is stable. The ideal duration of posttrauma monitoring is not precisely known. From data cited above, observation for 4 hours is reasonable with a normal tracing and no other sentinel findings such as contractions, uterine tenderness, or bleeding. Certainly, monitoring should be continued as long as there are uterine

contractions, nonreassuring fetal heart patterns, vaginal bleeding, uterine tenderness or irritability, serious maternal injury, or ruptured membranes (American College of Obstetricians and Gynecologists, 2017b). In rare cases, placental abruption has developed days after trauma (Higgins, 1984).

Fetal-Maternal Hemorrhage

It is unclear whether routine use of the Kleihauer-Betke or an equivalent test in pregnant trauma victims might modify adverse outcomes associated with fetal anemia, cardiac arrhythmias, and death (Pak, 1998). In a retrospective review of 125 pregnant women with blunt injuries, the Kleihauer-Betke test was judged to be of little value during acute trauma management (Towery, 1993). Others have reached similar conclusions, although a positive test with fetal cells of 0.1 percent was predictive of uterine contractions or preterm labor (Connolly, 1997; Muench, 2003, 2004).

For the woman who is D-negative, administration of anti-D immunoglobulin should be considered. This may be omitted if a test for fetal bleeding is negative. Even with anti-D immunoglobulin, alloimmunization may still develop if the fetal-maternal hemorrhage exceeds 15 mL of fetal cells (Chap. 15, Fetomaternal Hemorrhage).

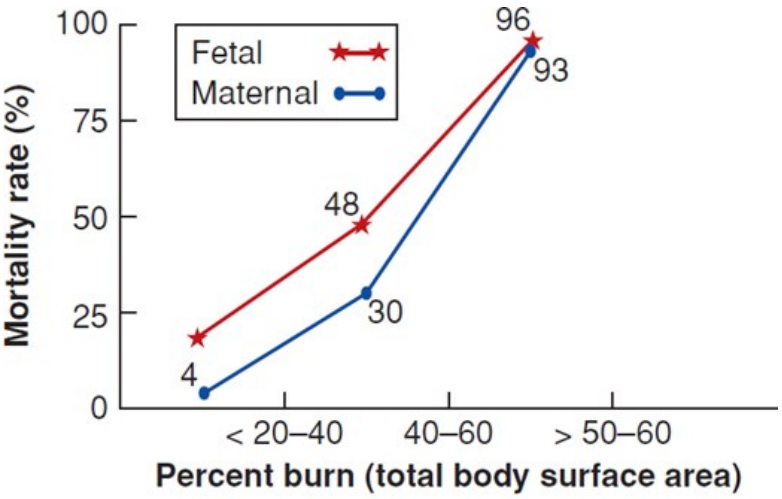
For the pregnant trauma patient, confirmation of current tetanus immunization status is pertinent. When indicated, a dose of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) is preferred for its neonatal pertussis immunity benefits (Chap. 9, Automobile and Air Travel).

THERMAL INJURY

Treatment of the burned gravida is similar to that for nonpregnant patients (Mendez-Figueroa, 2016). With treatment, it is generally agreed that pregnancy does not alter maternal outcome from thermal injury compared with that of nonpregnant women of similar age. As perhaps expected, maternal and fetal survival parallels the percentage of burned surface area (Parikh, 2015). Karimi and colleagues (2009) reported higher mortality rates for both with suicidal attempts and with inhalational injuries. The composite mortality rate for nearly 400 women from seven studies increased in a linear fashion as the percent of burned body surface area increased (Fig. 47-12). For 20-, 40-, and 60-percent burns, the maternal mortality rates were approximately 4, 30, and 93 percent, respectively. The corresponding fetal mortality rates were 20, 48, and 96 percent, respectively. With severe burns, the woman usually enters labor spontaneously within a few days to a week and often delivers a stillborn. Contributory factors are hypovolemia, pulmonary injury, septicemia, and the intensely catabolic state (Radosevich, 2013).

FIGURE 47-12

Maternal and fetal mortality rates by burn severity in nearly 400 women. (Data from Akhtar, 1994; Amy, 1985; Mabrouk, 1977; Maghsoudi, 2006; Parikh, 2015; Rayburn, 1984; Rode, 1990.)



Following serious abdominal burns, skin contractures that develop may be painful during a subsequent pregnancy and may even require surgical decompression and split-skin autografts (Mitsukawa, 2015; Radosevich, 2013). Loss or distortion of nipples may cause problems in breastfeeding. Mitsukawa and associates (2015) reported that contracture release was indicated with scars spanning more than >75 percent of the total abdominal

area. Alternatively, normal abdominal tissue expansion due to pregnancy appears to be an excellent source for obtaining skin grafts postpartum to correct scar deformities at other body sites (Del Frari, 2004).

Electrical and Lightning Injuries

Earlier case reports suggested a high fetal mortality rate with electric shock (Fatovich, 1993). In a prospective cohort study, however, Einarson and coworkers (1997) showed similar perinatal outcomes in 31 injured women compared with those of noninjured controls. They concluded that traditional 110-volt North American electrical current likely is less dangerous than the 220-volt currents available in Europe. A woman with iliofemoral thrombosis at 29 weeks' gestation that *may* have been related to a mild electrical shock at 22 weeks was described (Sozen, 2004). Another woman with brain death from cardiac arrest was reported (Sparic, 2014). Thermal burns with electrocution may be extensive.

The pathophysiological effects of lightning injuries can be devastating. García Gutiérrez and coworkers (2005) reviewed 13 case reports of lightning injuries during pregnancy and cited a 50-percent stillbirth rate.

CARDIOPULMONARY RESUSCITATION

According to estimates from the Nationwide Inpatient Sample, cardiac arrest complicates approximately 1 in 12,000 delivery admissions (Mhyre, 2014). The most common underlying causes were hemorrhage, heart failure, amnionic-fluid embolism, and sepsis. General topics regarding planning and equipment have been reviewed by the American College of Obstetricians and Gynecologists (2017b) and the Society for Obstetric Anesthesia and Perinatology (Lipman, 2014). Special considerations for cardiopulmonary resuscitation (CPR) conducted in the second half of pregnancy are outlined in the American Heart Association 2010 guidelines (Jeejeebhoy, 2015). The committee acknowledges the following as standards for critically ill gravidas: (1) relieve possible vena caval compression by left lateral uterine displacement, (2) administer 100-percent oxygen, (3) establish intravenous access above the diaphragm, (4) assess for hypotension that warrants therapy, which is defined as systolic blood pressure <100 mm Hg or <80 percent of baseline, and (5) review possible causes of critical illness and treat conditions as early as possible.

The position of the heart for external compressions is not different from that in nonpregnant women (Holmes, 2015). In nonpregnant women, external chest compression results in a cardiac output approximately 30 percent of normal. In late pregnancy, this may be even less with compressions because of uterine aortocaval compression (Clark, 1997; Nelson, 2015). Thus, it is paramount to accompany other resuscitative efforts with uterine displacement. This can be accomplished by tilting the operating table laterally, by placing a wedge under the patient's right hip, or by pushing the uterus to the left manually (Rees, 1988; Rose, 2015). If no equipment is available, an individual may kneel on the floor with the maternal back on his or her thighs to form a "human wedge" (Whitty, 2002).

Cesarean Delivery

During maternal resuscitation, because of pregnancy-induced hindrances on CPR efforts, emergent *perimortem cesarean delivery* for fetal salvage and improved maternal resuscitation may be considered. Some have stated that cesarean delivery is indicated within 4 to 5 minutes of beginning CPR if the fetus is viable (Drukker, 2014). In women delivered by perimortem cesarean, neurologically intact neonatal survival and the cardiac arrest-to-delivery interval are inversely related (Katz, 2012). Specifically, of newborns delivered within 5 minutes of arrest, 98 percent are neurologically intact; within 6 to 15 minutes, 83 percent are intact; within 16 to 25 minutes, 33 percent are intact; and within 26 to 35 minutes, only 25 percent are intact (Clark, 1997). This, coupled with some evidence that delivery *may* also enhance maternal resuscitation, has led the American College of Obstetricians and Gynecologists (2017b) to recommend *consideration* for cesarean delivery to begin within 4 minutes of cardiac arrest in these cases.

This serious and sometimes contentious issue is far from evidence based. To wit, Katz and associates (2005) reviewed 38 perimortem cesarean deliveries with a "large selection bias." They concluded that these reports supported—but "fell far from proving"—that perimortem cesarean delivery within 4 minutes of maternal cardiac arrest improves maternal and fetal outcomes. Even so, as emphasized by Clark (1997) and Rose (2015) and their coworkers, and in our experiences, these goals rarely can be met in actual practice. For example, most cases of cardiac arrest occur in uncontrolled circumstances, and thus, the time to CPR initiation alone would require the first 5 minutes. Thus "crash" cesarean delivery would supersede resuscitative efforts, would necessarily be done without appropriate anesthesia or surgical equipment, and more likely than not, would lead to maternal death. Moreover, the distinction between a perimortem versus postmortem cesarean operation is imperative (Katz, 2012; Rose, 2015). Last, in the balance, any choice *may* favor survival of the mother over the fetus, or vice versa, and thus there are immediate unresolvable ethical concerns. Katz (2012) has provided a scholarly review of perimortem cesarean delivery.

Maternal Brain Death

Occasionally, a pregnant woman with a supposedly healthy intact fetus will be kept on somatic support to await fetal viability or maturity. This is discussed in Chapter 60 (Idiopathic Intracranial Hypertension).

ENVENOMATION

According to their review, Brown and coworkers (2013b) reported that clinically significant envenomations in pregnant women are from snakes, spiders, scorpions, jellyfish, and hymenoptera such as bees, wasps, hornets, and ants. Adverse outcomes are related to maternal effects. These investigators conclude that limited evidence supports the use of a venom-specific approach that includes symptomatic care, antivenom administration when appropriate, anaphylaxis treatment, and fetal assessment. One management scheme for North American snakebites was provided by Lei and associates (2015).

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