Severe Sepsis and Septic Shock in Pregnancy

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Pregnancies complicated by severe sepsis and septic shock are associated with increased rates of preterm labor, fetal infection, and preterm delivery. Sepsis onset in pregnancy can be insidious, and patients may appear deceptively well before rapidly deteriorating with the development of septic shock, multiple organ dysfunction syndrome, or death. The outcome and survivability in severe sepsis and septic shock in pregnancy are improved with early detection, prompt recognition of the source of infection, and targeted therapy. This improvement can be achieved by formulating a stepwise approach that consists of early provision of time-sensitive interventions such as: aggressive hydration (20 mL/kg of normal saline over the first hour), initiation of appropriate empiric intravenous antibiotics (gentamicin, clindamycin, and penicillin) within 1 hour of diagnosis, central hemodynamic monitoring, and the involvement of infectious disease specialists and critical care specialists familiar with the physiologic changes in pregnancy. Thorough physical examination and imaging techniques or empiric exploratory laparotomy are suggested to identify the septic source. Even with appropriate antibiotic therapy, patients may continue to deteriorate unless septic foci (ie, abscess, necrotic tissue) are surgically excised. The decision for delivery in the setting of antepartum severe sepsis or septic shock can be challenging but must be based on gestational age, maternal status, and fetal status. The natural inclination is to proceed with emergent delivery for a concerning fetal status, but it is imperative to stabilize the mother first, because in doing so the fetal status will likewise improve. Prevention Aggressive treatment of sepsis can be expected to reduce the progression to severe sepsis and septic shock and prevention strategies can include preoperative skin preparations and prophylactic antibiotic therapy as well as appropriate immunizations.

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Sepsis is a leading cause of death in the United States and the number one cause of death in the intensive care unit, with a mortality rate of up to 29%.[1–3] The reported incidence is approximately 240–300 cases per 100,000 population, with over 750,000 cases per year and an expected increase by 1.5% each year.[1,4,5]

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In 1997, we[6] reviewed our experience in the treatment of 18 women diagnosed with septic shock during pregnancy or the immediate postpartum period. Our study and the multi-institutional review of 10 cases by Lee et al[7] constituted the limited case series reported in the U.S. obstetric literature for the previous two decades. Since our report, there has been a considerable effort to improve outcomes in sepsis with early goal-directed therapy in the medical and surgical populations.[8–11] The purpose of this report is to review the recent literature in the terminology, incidence, etiology, diagnosis, management, outcome, and prevention of severe sepsis and septic shock complicating pregnancy.

TERMINOLOGY

Historically, studies involving patients with sepsis were flawed by imprecise definitions for sepsis and its spectrum of clinical presentations. In 1992, the American College of Chest Physicians and the Society of

Critical Care Medicine published guidelines to standardize the definition for sepsis-related disorders[12] and a subsequent consensus conference was held in 2001 to "revisit the definitions for sepsis and related conditions" in an effort to review and improve on the current definitions.[9] The term "systemic inflammatory response syndrome (SIRS)" was used to describe the inflammatory process that can be generated by infection or by noninfectious causes such as pancreatitis, burns, and trauma. In nonpregnancy, SIRS is defined as the presence of two or more of the following: temperature greater than 38°C or less than 36°C, heart rate greater than 90 beats/min, respiratory rate greater than 20 breaths/min or $PaCO_2$ less than 32 mm Hg, and white blood cell count greater than 12,000/mm^3, less than 4,000/mm^3, or greater than 10% immature (band) forms.[9,12]

Sepsis is SIRS resulting from infection. Severe sepsis is sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Septic shock is a subset of severe sepsis defined as sepsis-induced hypotension persisting despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status. The term multiple organ dysfunction syndrome was introduced to define the presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention.[12]

These criteria are based on vital signs, white blood count, and organ dysfunction. They are used in nonpregnant adults to guide admission to the intensive care unit and treatment as well as to predict mortality and serious morbidity. Each level of disease correlates with prognosis, because mortality increases with progression from SIRS to septic shock in nonpregnant adults.[9,13] These guidelines, however, have never been validated in pregnant or postpartum women.

In general, obstetric patients with sepsis-related disorders tend to be a younger, healthier population and with proper treatment have a less morbid course with decreased mortality rates than nonpregnant, critically ill adults.[6,14–18] Severe sepsis and septic shock, however, remain important contributors to maternal mortality. Indeed, despite a decline in the overall UK maternal mortality rate, there has been an increase in deaths related to genital tract sepsis, particularly from community-acquired group A streptococcal disease.[19] The mortality rate related to sepsis increased from 0.85 deaths per 100,000 maternities in 2003–2005 to 1.13 deaths in 2006–2008, and sepsis is now the most common cause of direct maternal death in the United Kingdom.[19]

Accurate identification of those at risk for deterioration is difficult secondary to the normal alteration in physiology and the infrequency of septic shock in pregnancy. Physicians caring for critically ill, nonpregnant adults have used various standardized scoring systems to classify disease severity and to assist in identifying inpatients who are at risk for catastrophic decompensation from sepsis. An example includes the Modified Early Warning Score for medical emergency admissions to identify patients at risk for death and intensive care unit (ICU) admission. The score was validated by Subbe et al.[20] Some of these scoring systems have been evaluated in the obstetric population but were found to be unreliable or to overpredict risk of mortality.[16–19] Lappen et al[17] retrospectively evaluated 913 patients with chorioamnionitis (of whom, 575 met SIRS criteria) to decide if the SIRS criteria and Modified Early Warning Score could be used to predict sepsis, ICU transfer, or death. They concluded that neither adequately identified obstetric patients at risk.[17]

INCIDENCE

Literature highlighting sepsis in pregnancy is sparse and based mostly on case studies or retrospective studies with small numbers. Fortunately, septic shock is rare in pregnancy, occurring in 0.002–0.01% of all deliveries, and only 0.3–0.6% of reported patients with sepsis are pregnant.[2,5,6] Even in obstetric patients with documented bacteremia, septic shock has only been observed to occur in 0–12% of these cases.[21–23]

The incidence of acute medical and surgical emergencies in pregnancy and postpartum leading to rises of severe sepsis and septic shock has increased during the past decade and is expected to continue to increase in the future. This increase has resulted from the change in demographics of women who are pregnant as well as the change in obstetric practice. Pregnancies in women 40 years and older are much more common than a decade ago. With advanced maternal age, there are increased rates of obesity, type 2 diabetes mellitus, placenta previa, and abruptio placentae.[24] The availability of assisted reproductive technologies also has had an effect because these women are more likely to have multifetal gestation. Furthermore, patients with multifetal gestation are more likely to require invasive diagnostic and therapeutic procedures such as cervical cerclage, serial amnioreduction, fetal or placental surgery, with any of these procedures associated with an increased rate of septic complications.[25,26]

The percentage of pregnant women who are obese or morbidly obese has also increased during the past decade. Obesity is associated with increased incidence of hypertensive disorders of pregnancy, type 2 diabetes mellitus, cesarean delivery, and cardiopulmonary complications.[27] Obese women also have increased tissue hypoxia as a result of the decreased vascularity of the subcutaneous fat, as well as having an increased risk for hematoma or seroma formation, which combined increases the risk for septic complications.

ETIOLOGY

The etiology of severe sepsis and septic shock during pregnancy and postpartum can be the result of either obstetric-related or nonobstetric-related conditions. Potential causes of severe sepsis or septic shock during pregnancy and the puerperium are listed in Box 1.

Box 1. Causes of Severe Sepsis and Septic Shock in Pregnancy and the Puerperium

- Acute pyelonephritis
- Retained products of conception
  - Septic abortion
  - Conservative management of placenta accreta or percreta
- Neglected chorioamnionitis or endomyometritis
  - Uterine microabscess or necrotizing myometritis
  - Gas gangrene
  - Pelvic abscess
- Pneumonia
  - Bacterial examples
    - Staphylococcus
    - Pneumococcus
    - Mycoplasma
    - Legionella
  - Viral examples
    - Influenza
      - H1N1
    - Herpes
    - Varicella
- Unrecognized or inadequately treated necrotizing fasciitis
  - Abdominal incision
  - Episiotomy
  - Perineal laceration
- Intraperitoneal etiology (nonobstetric)
  - Ruptured appendix or acute appendicitis
  - Bowel infarction
  - Acute cholecystitis
  - Necrotizing pancreatitis

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DIAGNOSIS

Alterations in physiology surrounding pregnancy are characterized by substantial changes in maternal hemodynamics[28] as well as respiratory and renal function. They are further influenced by conditions associated with intrapartum and postpartum blood loss, common infections such as chorioamnionitis, endometritis, pneumonia, pyelonephritis, use of fluids, medications, delivery mode, and anesthesia. These factors influence vital signs and laboratory evaluations and make accurate diagnosis of severe sepsis and septic shock more difficult in the obstetric patient, particularly during labor because heart rate and respiration rates increase.[3]

The presenting signs and symptoms in severe sepsis during pregnancy can be variable and can differ from the nonpregnant state depending on the etiology as well as the duration of infection[2,6,7,29–34] (Box 2). The most common presenting symptom in pregnancy and the puerperium is fever (greater than 38°C or greater than 100.4°F) with or without chills; however, in cases of advanced sepsis, the patient can develop hypothermia (temperature less than 36°C [less than 96.8°F]) with tachycardia (heart rate greater than 110 beats/min) and tachypnea (respiratory rate greater than 24/min). In most cases, the location of pain or tenderness will assist in determining the etiology of the underlying infection. For example, patients with pyelonephritis will present with flank or back pain and the tenderness will localize at the costovertebral angle,[35] whereas those presenting with cholecystitis, appendicitis, or pancreatitis will have mid-quadrant or right upper quadrant abdominal pain and tenderness or generalized abdominal pain.[32,36] The physical and clinical findings for infections common in pregnancy and postpartum are discussed subsequently. The diagnosis and management of nonobstetric intraperitoneal etiologies of severe sepsis or septic shock complicating pregnancy including acute appendicitis,[31,32] acute cholecystitis,[32] and pancreatitis[36] are beyond the scope of this article but have recently been reviewed elsewhere.

Pyelonephritis

Early clinical signs of pyelonephritis can include fever, chills, dysuria, flank pain, nausea, and vomiting. Physical examination is notable for costovertebral angle tenderness and severe flank pain. Initial evaluation should include complete blood count, urinalysis, and urine culture. The diagnosis of acute pyelonephritis in pregnancy includes the clinical findings of fever (temperature 38.0°C or greater), flank pain and costovertebral angle tenderness, and the

Box 2. Clinical and Laboratory Findings of Severe Sepsis and Septic Shock

Signs and Symptoms

- Fever
- Temperature instability (higher than 38.0°C or lower than 36.0°C)
- Tachycardia (heart rate greater than 110 beats/min)
- Tachypnea (respiratory rate greater than 24 beats/min)
- Diaphoresis
- Clammy or mottled skin
- Nausea or vomiting
- Hypotension or shock
- Oliguria or anuria
- Pain (location based on site of infection)
- Altered mental state (confusion, decreased alertness)

Laboratory Findings

- Leukocytosis or leukopenia
- Positive culture from infection site or blood, or infection site and blood
- Hypoxemia
- Thrombocytopenia
- Metabolic acidosis
  - Increased serum lactate
  - Low arterial pH
  - Increased base deficit
- Elevated serum creatinine
- Elevated liver enzymes
- Hyperglycemia in the absence of diabetes
- Disseminated intravascular coagulation

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laboratory findings of either bacteriuria (20 bacteria per high-powered field) or pyuria.[35] The most common etiologies are Gram-negative bacilli such as *Escherichia coli* or *Klebsiella* species and Gram-positive organisms including group B streptococci.[35] A high frequency of antibiotic-resistant organisms is common in hospitalized patients if they have had prolonged indwelling urinary catheterization.

Acute respiratory insufficiency was present in 7% of the 440 cases of antepartum pyelonephritis reported by Hill et al.[35] Patients with acute respiratory insufficiency had more pronounced tachycardia, anemia, renal dysfunction, and higher fevers than those without respiratory insufficiency.[35] Patients with pyelonephritis with shortness of air or with decreased oxygen saturations by pulse oximetry should be evaluated with a chest radiograph. In those failing initial antibiotic therapy, imaging including renal ultrasonogram or magnetic resonance imaging to assess for underlying pathology including hydronephrosis (Fig. 1), presence of nephrolithiasis, lobar nephronia (focal infection), abscess, or obstruction is indicated.

Septic Abortion

Septic abortion can occur after an incomplete spontaneous miscarriage or incomplete surgical or medical elective abortion. Early clinical signs can include high fever, chills, foul-smelling vaginal discharge, and severe abdominal pain, cramping, or both. Physical examination is notable for uterine and abdominal tenderness. Initial evaluation should include pelvic examination, cervical cultures, and ultrasonographic imaging. Uterine evacuation after administration of broad-spectrum antibiotics is necessary to remove all remaining infected products of conception. Patients are also at risk for infection extending beyond the uterus including parametritis and peritonitis. Certain cases will not respond adequately to antibiotic therapy and will require imaging or surgical evaluation for the presence of pelvic abscess or necrotizing myometritis.

Chorioamnionitis and Endomyometritis

Bacterial organisms of the lower genital tract may ascend into the lower uterine segment during labor or

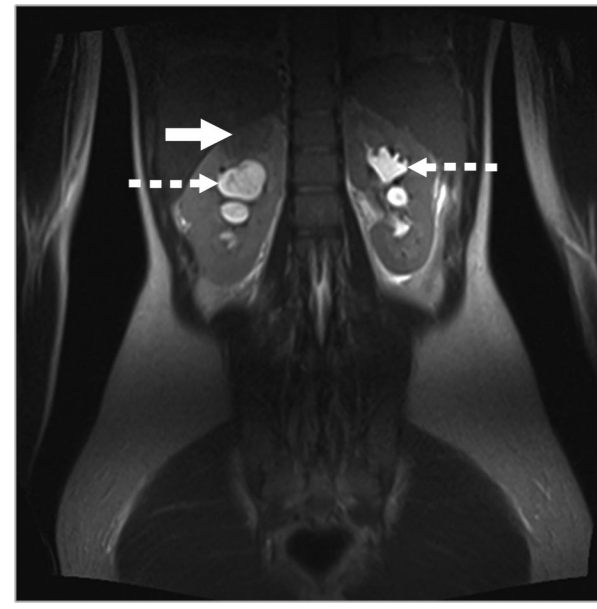

Fig. 1. Abdominal magnetic resonance imaging scan revealing substantial obstructive hydronephrosis of the kidneys (*broken arrows*), right kidney greater than left. Signal distortion in the superior portion of the right renal parenchyma suggests acute lobar nephronia (focal infection without liquefaction) and pyelonephritis (*solid arrow*).
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after rupture of membranes resulting in infection of the chorion, amnion, and ultimately the fetus. Early clinical signs of chorioamnionitis can include fever, maternal or fetal tachycardia or both, uterine tenderness, change in amniotic fluid color to yellow or green, and purulent vaginal drainage. After delivery, patients diagnosed with chorioamnionitis remain at risk for continued sepsis, especially if they require cesarean delivery, because a hysterotomy repair will create a local anaerobic environment along the suture line. If patients remain febrile after delivery despite appropriate and adequate antibiotic therapy, a thorough examination is indicated to assess for pelvic abscess or necrotizing myometritis as well as for potential remote sites of infection such as pneumonia, retained surgical sponge or instrument, wound infection, and septic pelvic thrombophlebitis.

Before the advent of antibiotic therapy and sterile technique, group A β-hemolytic *Streptococcus* (*Streptococcus pyogenes*) was a major microbial cause of postpartum infection[37] and the infectious agent responsible for childbed or puerperal fever. Group A *Streptococcus* species can cause a diverse variety of infections in the obstetric patient, including endomyometritis, necrotizing fasciitis, pneumonia, cellulitis, and pharyngitis. The clinical findings of necrotizing myometritis from group A *Streptococcus* infection may include a uterus that is boggy on examination and edematous on visual inspection.[38] Uterine tenderness may be absent because the uterus is necrotic and has diminished innervation. Pelvic imaging may have diminished benefit in this situation.

Obstetric patients appear especially vulnerable to group A *Streptococcus* infections acquired through disruption of mucosal or cutaneous barriers during delivery.[39] As reviewed by de Moya et al,[40] the systemic toxicity seen in patients with group A *Streptococcus* infection appears to be the result of both endotoxins produced by the bacteria and streptococcal proteins stimulating the T-cell-mediated release of cytokines.[40] As a result, group A *Streptococcus* infections can rapidly progress to a multiorgan infection with high mortality.[6,41] Surgical management of the source of infection (hysterectomy) is instrumental to improve outcome by decreasing the bacterial load and improving antibiotic effectiveness.[38,40]

Pneumonia

The physiologic changes during pregnancy in the respiratory system are beneficial to the fetus. In the setting of sepsis or septic shock, however, they increase the risk for severe pulmonary infections and exacerbate the clinical course of infection.[42] Specifically, pregnant women with pulmonary infection are predisposed to rapid declines in oxygenation and reduced ability to compensate for metabolic acidosis.[43]

The single most common community-acquired pathogen for pneumonia in pregnancy is *Streptococcus pneumoniae*.[42] Usually patients present with high fever and copious production of rusty-appearing purulent sputum. In contrast, patients with *Mycoplasma pneumoniae* have a more insidious onset, a dry paroxysmal cough, and may have extra pulmonary manifestations including myocarditis, pericarditis, and vasculitis or thrombosis. The clinical findings of viral pneumonia include dry cough, headache, and muscle pain. Rales may be heard over the affected lung segment and pulse oximetry will frequently reveal low oxygen saturation. A chest radiograph should be obtained to confirm the diagnosis. Pneumococcal pneumonia usually presents with segmental lobe infiltrates, whereas diffuse infiltrates are more common with *M pneumoniae* (Fig. 2) and viral pneumonias (Fig. 3).

Viral Pneumonia

The most common viral pathogens for pneumonia in pregnancy are influenza A and B. Although less common, varicella zoster virus can occur in pregnancy and is associated with mortality rates of 3–14% in patients who require mechanical ventilation, even with aggressive antiviral therapy.[44] Chest radiographic findings for viral pneumonia usually include nodular and interstitial infiltrates (Fig. 3). Infections may progress to acute

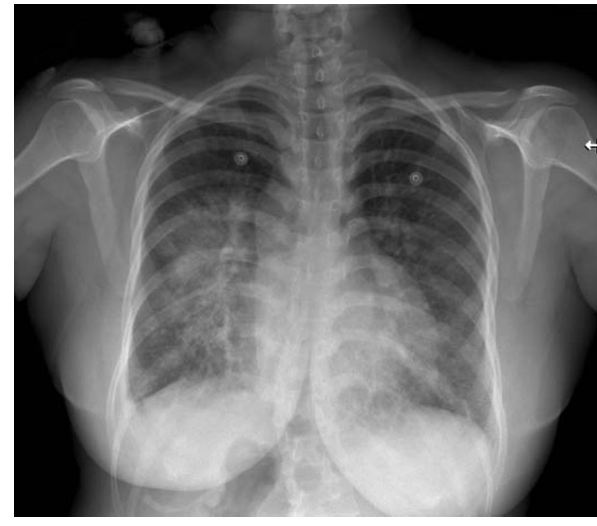

Fig. 2. Chest radiograph revealing bilateral pulmonary opacities and severe air-space disease with perihilar, midlung, and bilateral lower lung infiltrates, greater on the right.

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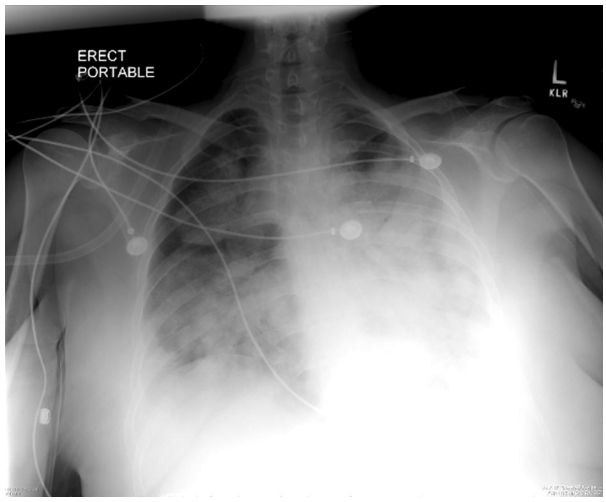

Fig. 3. Chest radiograph revealing extensive bilateral pulmonary infiltrates in a patient with H1N1 influenza pneumonia.

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respiratory decompensation, respiratory failure, or acute respiratory distress syndrome.

In patients with influenza during pregnancy, antiviral treatment should be started as soon as possible after illness onset, ideally within 48 hours of symptom onset.[45] Specifically, antiviral treatment of pregnant women with influenza A (2009 H1N1) has been shown to be most beneficial in preventing respiratory failure and death when started within less than 3 days of illness onset but still provided benefit when started 3–4 days after onset compared with 5 days or more.[46] Treatment with 75 mg oseltamivir twice daily or 10 mg zanamivir (two inhalations) twice daily for 5 days should not wait for laboratory confirmation of influenza. Longer treatment courses for patients who remain severely ill after 5 days of treatment can be considered.

Necrotizing Fasciitis and Necrotizing Vulvitis

Necrotizing fasciitis is a rapidly spreading bacterial infection of the soft tissue in which the major distinguishing characteristic is the presence of extensive necrosis and undermining of the skin with involvement of tissues up to and including the deep fascia. The typical signs are erythema, purplish discoloration of the skin with bullae, edema, crepitus, and pain that seems disproportionate to the findings on examination.[40] Most importantly, the degree of tissue necrosis cannot be predicted by simple visual evaluation of the cutaneous signs. Although initially painful, later signs of necrotizing fasciitis include skin discoloration and local analgesia resulting from disruption in blood supply and innervation. The infection is usually polymicrobial, and the major organisms include group A *Streptococcus* species, *Staphylococcus aureus,* and *Clostridium perfringens.*

As noted by Stephenson et al,[47] the absence of visual purulent material does not exclude the diagnosis of necrotizing fasciitis. Crepitus can also be a late sign resulting from gas-forming anaerobic bacteria within the ischemic tissues,[47] and radiographic or computed tomographic imaging can show subcutaneous gas suggestive of a clostridial infection. As reviewed by de Moya et al,[40] the histopathologic criteria for the diagnosis of necrotizing fasciitis include dermal edema and necrosis, fascial necrosis, and interstitial fibrin; the presence of neutrophils, lobular panniculitis, inflammation, and thrombosis of blood vessels; and the presence of abundant micro-organisms but sparing of the deep striated muscle.

Necrotizing vulvitis can occur at the episiotomy site or at a site of perineal laceration and is characterized by progressive, often rapid inflammation and extensive necrosis of subcutaneous tissue including the fascia and adjacent tissues.[47] The microbiology is similar to necrotizing fasciitis of the abdominal wall but symptoms may be delayed or ignored given postpartum discomfort after vaginal delivery. Although postpartum perineal discomfort is common after vaginal delivery, especially with vaginal lacerations, it is prudent to perform a detailed examination for labial cellulitis.

LABORATORY FINDINGS

Laboratory findings in severe sepsis or septic shock will depend on the etiology, the duration of infection, presence of pre-existing medical or obstetric disorders, and the quality of management used.[2,6,7,29–34] (Box 2). It is important to note that traditional laboratory values to define sepsis in nonpregnant women may not apply to pregnancy. The most common laboratory abnormality in patients with septic shock during pregnancy is leukocytosis (usually a white blood count greater than 15,000/mm^3); however, in cases of advanced sepsis, the patient can develop leukopenia and neutropenia as a result of bone marrow suppression. In addition, patients with viral sepsis will usually have leukopenia. Moreover, most patients will have serum creatinine levels greater than 1.0 mg/dL (88 micromoles/L), which are abnormal values for pregnancy.[48]

In nonpregnant individuals, a serum lactate level of greater than 4.0 mmol/L strongly correlates with extensive tissue hypoxia, anaerobic metabolism re-

sulting from hypoperfusion, and a diagnosis of severe sepsis. In a study by Mikkelsen et al,[49] intermediate (2.0–3.9 mmol/L) and high (greater than 4.0 mmol/L) serum lactate levels correlated with increased mortality independent of organ failure and shock.[49] Furthermore, early lactate clearance has been associated with improved outcome in severe sepsis and septic shock.[50] The use of serum lactate levels in the diagnosis of severe sepsis and septic shock and correlation with risk of mortality in pregnancy, however, is unknown.

MATERNAL AND PERINATAL COMPLICATIONS

The reported incidences of serious acute maternal morbidity as the result of severe sepsis in a European population-based study (MOMS-B survey) ranged from 0.0 to 4.0 per 1,000 deliveries.[51] This incidence of serious acute maternal morbidity was comparable to previous reports from the United States (0.4–0.6 per 1,000)[52,53] and Canada (0.1–0.3 per 1,000).[54,55] Pregnancies complicated by severe sepsis or septic shock are associated with increased rates of preterm labor, fetal infection, operative delivery, and preterm delivery resulting in increased rates of perinatal morbidity and mortality. Kankuri et al[56] noted that preterm deliveries were associated with a crude 2.7-fold risk for peripartum sepsis as compared with term deliveries. Furthermore, antepartum sepsis was associated with a crude 2.6-fold risk for cesarean delivery, whereas postpartum sepsis was 3.2 times more likely to occur after cesarean delivery than after vaginal delivery.[56] In 74 obstetric patients admitted to ICUs, Afessa et al[14] found rates of 59%, 24%, and 3%, respectively, for SIRS, severe sepsis, and septic shock. They noted patients admitted to the ICU with SIRS had longer ICU stays, longer hospital stays, and were more likely to develop organ failure than those admitted to the ICU without SIRS.

Although septic shock is rare during pregnancy, its development may result in substantial maternal morbidities and even maternal death (Box 3). In 18 obstetric patients with septic shock reported by Mabie et al,[6] the majority of patients had depressed left ventricular function. Myocardial dysfunction in sepsis is poorly understood but appears to be related to several circulating myocardial depressant substances, one of which is tumor necrosis factor. Other indicators that suggest a poor outcome in patients with established septic shock are presented in Box 4. Maternal mortality rates in previously reported studies found a 12% overall mortality in septic patients admitted to the ICU[18] and 20–28% mortality in those with septic shock,[6,7] with the highest rates seen in patients with multiple organ dysfunction syndrome.[6] This mortality rate is similar to our most recent experience in 10 patients with septic shock in which there were three maternal deaths. All three deaths had multiorgan failure involving six or more organ systems. Furthermore, in each of the maternal deaths, a delay in aggressive treatment was identified before transfer to the tertiary care center (unpublished data).

Box 3. Maternal and Perinatal Complications of Severe Sepsis and Septic Shock

Maternal
- Admission to intensive care unit
- Pulmonary edema
- Adult respiratory distress syndrome
- Acute renal failure
- Shock liver
- Septic emboli to other organs
- Myocardial ischemia
- Cerebral ischemia
- Disseminated intravascular coagulation
- Death

Perinatal
- Preterm delivery
- Neonatal sepsis
- Perinatal hypoxia or acidosis
- Fetal or neonatal death

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MANAGEMENT

Early detection of the disease process and intervention can improve the outcome and survivability in

Box 4. Prognostic Indicators of Poor Outcome in Septic Shock

- Delay in initial diagnosis
- Pre-existing debilitating disease process
- Poor response to massive intravenous fluid resuscitation
- Depressed cardiac output
- Reduced oxygen extraction
- High serum lactate (greater than 4 mmol/L)
- Multiple organ dysfunction syndrome

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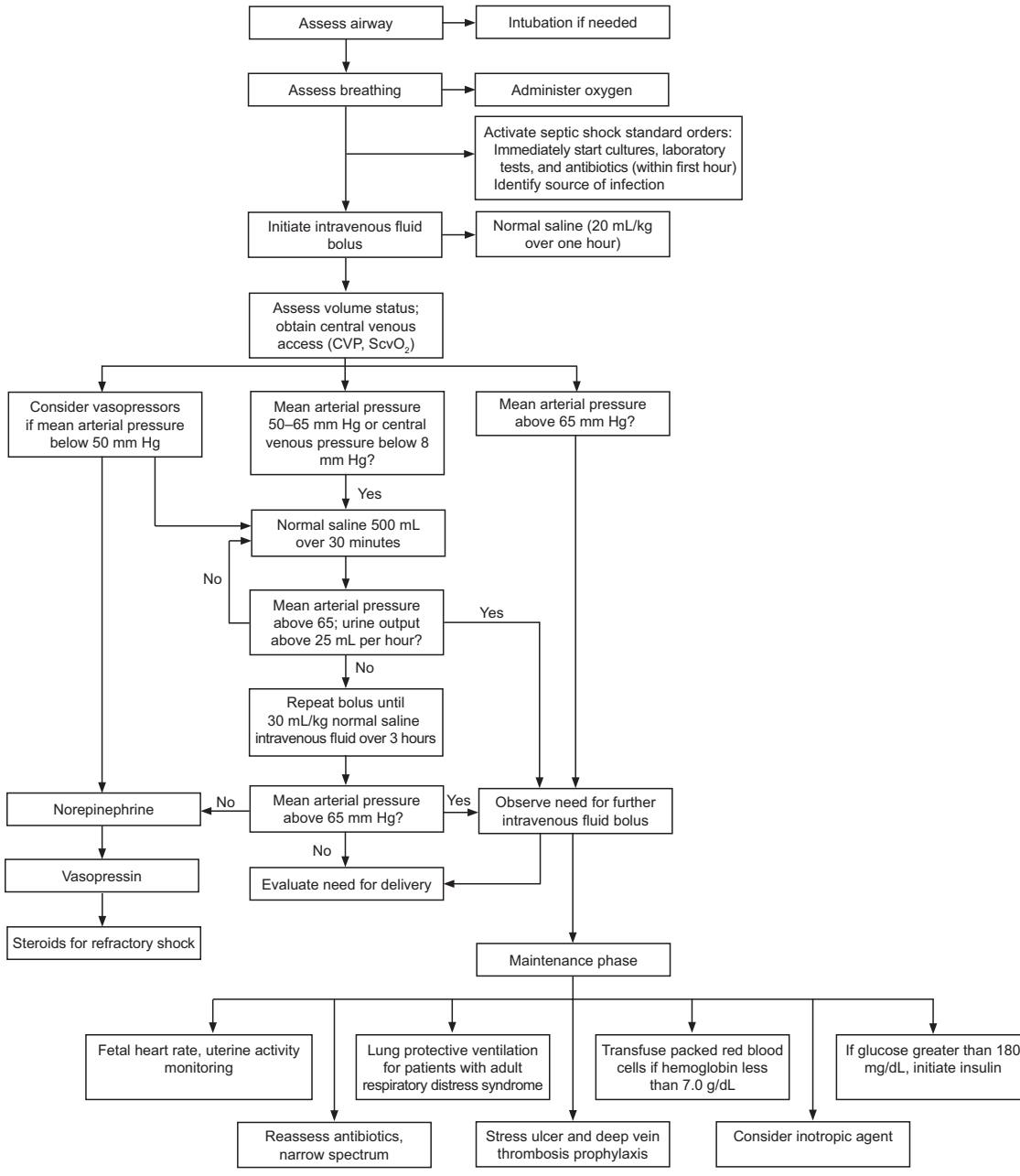

Fig. 4. An algorithm of management for septic shock in pregnancy. Data from: Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368–77. CVP, central venous pressure; $ScvO_2$, central venous oxygen saturation.

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severe sepsis and septic shock. Early provisions of time-sensitive therapies and standardized therapies of best practice have been shown to decrease mortality, hospital cost, and hospital length of stay in randomized studies in complicated nonpregnant patients.[8,10,11,13] This finding underscores the importance of developing and implementing a severe sepsis protocol that includes goal-directed therapy. This requires the involvement of a multidisciplinary approach that includes physicians, nursing, pharmacy, and hospital administration staff. Most of these patients will require ICU admission. Although high-intensity ICU physician staffing (mandatory intensivist consultation) has been associated with lower ICU mortality and decreased ICU length of stay compared with low-intensity ICU physician staffing (optional intensivist consultation),[57] it is

important for the obstetric team to remain involved to address the unique management issues of pregnancy and the puerperium.

Initial Resuscitation Phase

Figure 4 depicts a suggested algorithm of management for septic shock in pregnancy. With any critically ill patient, the initial treatment should include assuring adequate oxygenation and respiratory effort. Supplemental oxygen should be provided as directed by continuous pulse oximetry with arterial blood gas determinations performed as indicated. Ventilatory assistance may be required and intubation performed as necessary. Intravenous access should be obtained for fluid resuscitation and antibiotic therapy as soon as possible. Appropriate cultures should be obtained from likely sources of infection (including blood cultures) and broad-spectrum antibiotic therapy initiated within 1 hour. Initial laboratory evaluation should include a complete blood count, a comprehensive metabolic panel, serum lactate, coagulation studies, arterial blood gas, and urinalysis.

An initial step in goal-directed therapy is to identify sepsis and the site of infection. If septic shock is diagnosed, the physician should then activate Septic Shock Standard Orders (Box 5). Numerous studies have now shown that early goal-directed therapy in the treatment of severe sepsis and septic shock is associated with improved outcome and survival compared with traditional treatment.[8,11,13] Therapy goals in the management of severe sepsis and septic shock are outlined in Box 5.

Hemodynamic Management

In patients presenting with severe sepsis in association with hypotension, fluid resuscitation should be performed initially as rapid infusions of warmed fluids (500-mL bolus every 15 minutes with a goal of 20 mL/kg over the first hour of treatment) to optimize cardiac preload, afterload, and contractility. Subsequent intravenous infusions are guided by maternal vital signs, pulse oximetry, central hemodynamic monitoring, and urine output to avoid the development of pulmonary edema. Physiologic perfusion end points include a mean arterial pressure of 65 mm Hg or greater, central venous pressure 8–12 mm Hg, and a urine output greater than 25 mL/h. Colloids do not appear to be superior to crystalloids[58] but attempts should be made to avoid excess free water (ie, with use of 0.9% normal saline or lactated Ringer's).

Central venous access for measurement of central venous pressure and central venous oxygen saturation is recommended for patients with severe sepsis and septic shock. This monitoring can guide fluid therapy and warn of impending volume overload. Central venous oxygen saturation measures the oxygen saturation in venous blood returning to the heart, which reflects the balance between systemic oxygen delivery and oxygen consumption and can be monitored intermittently or with continuous central venous oxygen saturation assessment. A decrease in central venous oxygen saturation can be a marker for increased oxygen consumption (hyperthermia, stress) or decreased oxygen delivery (hypoxia, low cardiac output, anemia). Recent meta-analysis suggests that pulmonary artery catheters are of no added benefit and may possibly cause harm.[59]

When appropriate fluid resuscitation fails to resolve hypoperfusion or in patients with profound hypotension at presentation (mean arterial pressure less than 50 mm Hg), vasopressor therapy is indicated (Fig. 4). The goals of such therapy in shock are to restore effective tissue perfusion and normalize cellular metabolism.[60] Objective evidence of increased perfusion includes improvement in urine output, capillary refill, mental status, and fetal status. Norepinephrine is the first-line vasoactive therapy in septic shock. It increases mean arterial pressure by significant α-1 receptor-mediated vasoconstriction. Although norepinephrine can reduce uterine blood flow, this risk is outweighed by the benefit of maternal resuscitation. In a randomized trial comparing vasopressor agents to achieve and maintain normal hemodynamic and oxygen transport parameters for at least 6 hours in patients with volume-resuscitated sepsis, norepinephrine improved hemodynamics and oxygen delivery in 93% of patients compared with only 31% in patients treated with dopamine.[61] Furthermore, in the setting of septic shock, norepinephrine effectively decreased lactate levels and was associated with improved urine output.[62,63] In contrast, when dopamine is used as first-line therapy in septic shock, it increased sedation requirements and ventilator duration and was associated with more arrhythmias.[64] Low-dose dopamine infusion was previously recommended for renal-enhancing effects; however, recent trials have disputed this benefit.[65] In patients with hypotension refractory to fluid resuscitation and norepinephrine therapy, vasopressin has been reported to improve mean arterial pressure and renal function.[66]

Antimicrobial Therapy

Infections in obstetric patients tend to be polymicrobial, and many organisms are part of the normal vaginal flora. The most frequent organisms include groups A, B, and G streptococci, *E coli*, *Streptococci*

Box 5. Septic Shock Management

Initial Resuscitation Phase (first 6 h)
- Blood cultures obtained (goal within 1 h)
- Empiric antibiotics initiated (goal within 1 h)
- Central line placed (goal within 4 h)
- Central venous pressure 8 mm Hg or higher (goal within 6 h)
- Norepinephrine infusion if indicated (mean arterial pressure lower than 65 mm Hg after resuscitation)
- Transfusion of packed red blood cells if indicated by hemoglobin less than 7 g/dL

Hemodynamic Management
- Central line and arterial line placement
- Fluid resuscitation
  - Use warm normal saline or lactated Ringer's
  - Rapid infusion (500 mL over 15 min)
    - 1-h goal: total 20 mL/kg
    - 3-h goal: total 30 mL/kg
  - Physiologic perfusion end points
    - Central venous pressure 8–12 mm Hg
    - Mean arterial pressure greater than 65 mm Hg
    - Urine output greater than 25 mL/h
- Vasopressor therapy
  - Vasoactive agents if mean arterial pressure lower than 65 mm Hg after fluid resuscitation
  - Inotropes if central venous oxygen saturation remains less than 70%
  - Vasopressin if vasopressor therapy ineffective
- Oxygen therapy
  - Supplement with nasal cannula, face mask
  - Intubate, mechanical ventilation, if respiratory failure
    - Sedation, analgesia, neuromuscular blocker

Antimicrobial Therapy
- Prompt cultures
  - Do not delay therapy while awaiting cultures
  - Survival differences seen in delay of antibiotic therapy of only 1 h
- Prompt empiric antibiotic therapy
  - Gentamicin at 1.5 mg/kg intravenously, then 1 mg/kg intravenously every 8 h
  - Clindamycin at 900 mg intravenously every 8 h
  - Penicillin at 3,000,000 units intravenously every 4 h
    - or
  - Vancomycin at 15 mg/kg intravenously and then dosing by pharmacy
  - Piperacillin and tazobactam at 4.5 g intravenously every 6 h

Search and Eliminate Source of Sepsis
- Retained products of conception or necrotic uterus
- Débridement of infected tissue (incision, episiotomy, fascia)
- Abscess
- Pyuria with ureteral obstruction
- Appendicitis, cholecystitis, or pancreatitis

Box 5. Septic Shock Management (*continued*)

Maintenance Phase
- Insulin protocol initiated, if indicated
- Corticosteroid therapy for refractory septic shock
  - Hydrocortisone at 50 mg intravenously every 6 h
- Thromboembolic prophylaxis
  - Sequential compression device and
  - Enoxaparin at 40 mg subcutaneously once daily (or 5,000 units heparin subcutaneously every 8 h if hepatic or renal impairment)
- Stress ulcer prophylaxis
  - Famotidine at 20 mg every 12 h
- Reassess antibiotic therapy and narrow spectrum if possible

RBCs, red blood cells.

oralis, S aureus, and *Citrobacter* and *Fusobacterium* species.[34] The two most common bacterial etiologies of lethal peripartum sepsis identified, however, are group A β-hemolytic *Streptococcus* infection and *E coli*.[67] Any antimicrobial therapy chosen should provide broad-spectrum coverage for Gram-positive, Gram-negative, and anaerobic bacteria. Two commonly used broad-spectrum antibiotic regimes are presented in Box 5, but it is also advisable to consider local hospital antibiograms for antibiotic therapy in response to local resistance patterns. The choice of antibiotic can be refined once cultures and sensitivities are available. Frequent review of antimicrobial choice is important to minimize toxicity, optimize efficacy, and avoid developing antibiotic-resistant organisms. Although renal plasma flow and glomerular filtration rate are increased in pregnancy,[68] they are often adversely affected by severe sepsis and septic shock. Aminoglycoside drug levels should be monitored to ensure adequate therapy and to avoid toxicity.

Effective antimicrobial administration within the first hour of documented hypotension in septic shock has been associated with increased survival to hospital discharge in adult patients. Kumar et al[69] noted that for every additional hour to effective antimicrobial initiation in the first 6 hours after hypotension onset, survival dropped an average of 7.6%.[69] Delay in initiation of antimicrobial therapy has been associated in other studies with increased mortality in, for example, community-acquired pneumonia.[70,71]

The epidemiology of methicillin-resistant *S aureus* has changed in recent years. It is no longer a primarily hospital-acquired infection and is now a common community bacterial isolate. Current antibiotic recommendation for coverage of methicillin-resistant *S*

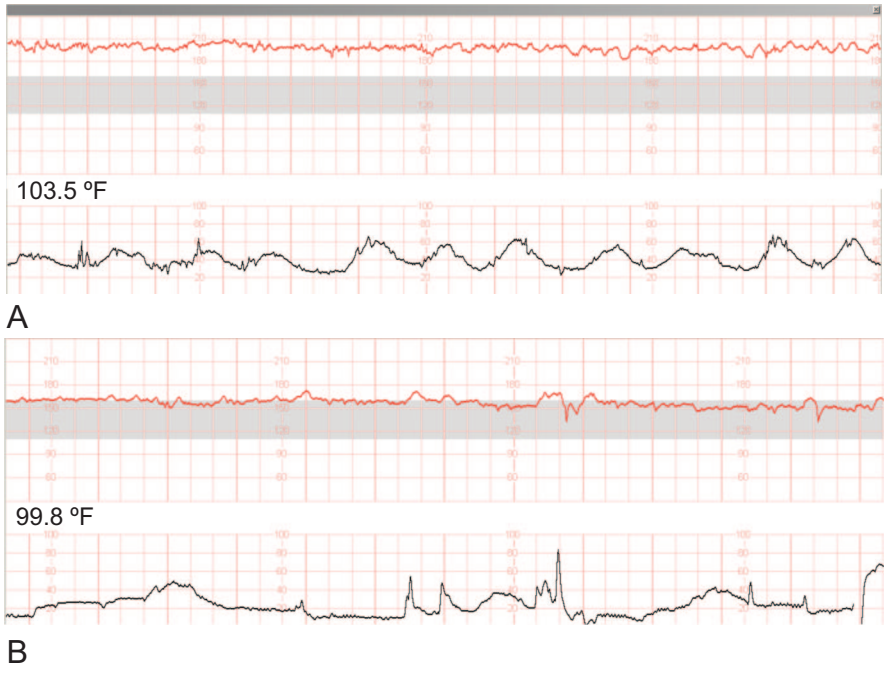

Fig. 5. A. Fetal monitoring in a patient with severe sepsis from pyelonephritis (temperature 103.5°F) revealing tachycardia and tachysystole. **B.** Subsequent fetal monitoring in the same patient with severe sepsis 3 hours after initiation of intravenous fluid bolus, acetaminophen, and intravenous antibiotic therapy (temperature 99.8°F) noting lower heart rate baseline and resolution of tachysystole.

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aureus would include vancomycin.[72] For patients with group A β-hemolytic *Streptococcus* infections that are not responding to antibiotic therapy, intravenous immunoglobulin has been advocated to improve bacterial clearance and neutralize circulating bacterial toxins.[41]

Antibiotic agents used in surgical prophylaxis (often cephalosporins) should be avoided when choosing an antimicrobial regimen for treatment of severe sepsis and septic shock because resistant organisms already may have been selected. In addition, cephalosporins will not provide adequate treatment for *Enterococcus* and *Listeria* infections.[67] Furthermore, a retrospective cohort study by Johnson et al[73] emphasized the importance of considering recent antibiotic exposure for treatment when formulating empiric antimicrobial regimens for suspected Gram-negative bacterial infection.

Fetal Evaluation

Fetal and tocodynamic monitoring are indicated at gestational ages compatible with the potential for extrauterine neonatal survival. Fetal heart rate monitoring in the setting of severe sepsis often reveals fetal tachycardia as a response to the maternal febrile episode (Fig. 5A). Furthermore, fetal heart rate variability may be minimal or absent with absent accelerations and often the development of decelerations. Tocodynamic monitoring may reveal tachystole as a result of irritation of the myometrium by purulent myometritis.[74]

Patients with acute infection during pregnancy can develop uterine contractions (with or without cervical change) as a result of release of endotoxins. In general, most patients will respond to hydration and the contractions will resolve after treatment. As a result, true preterm labor is not common. On occasion, however, a patient will develop true preterm labor with cervical dilatation suggesting the need for tocolytic therapy. A major concern with tocolytic therapy in this clinical setting is increasing the risk of pulmonary edema, particularly if β-agonists are used. Therefore, in certain instances such as gestational age less than 34 weeks, tocolytic therapy with magnesium sulfate to allow time for corticosteroid administration for fetal benefit may be considered. During a maternal febrile episode, fetal tachycardia will develop and, in fact, often precedes the maternal fever. Reduction in maternal body temperature with acetaminophen or a cooling blanket will decrease the need for the fetus to disperse heat through the placental circulation, thereby lowering the fetal heart rate baseline (Fig. 5B) and potentially improving the fetal metabolic status.

The decision for delivery in the setting of antepartum severe sepsis or septic shock can be challenging but must be based on gestational age, maternal status, and fetal status. The natural inclination is to proceed with emergent delivery for a concerning fetal status, but it is imperative to stabilize the mother first. In doing so, often the fetal status will likewise improve. Clinical situations for which delivery may likely be indicated to maximize the resuscitative

efforts in severe sepsis and septic shock are presented in Box 6. Anesthetic, surgical, and neonatal resuscitation equipment should be made available for both vaginal and operative delivery.[75] When vaginal delivery is planned, often an assisted second stage of labor will be needed as a result of limited maternal pushing effort resulting from compromised maternal respiratory or cardiac status. Secondary to increased oxygen consumption and reduced functional residual capacity of pregnancy compounded by the physiologic derangements with severe sepsis and septic shock, these patients are at risk for rapid deterioration in both maternal and fetal status requiring emergent delivery during hospitalization. Ideally, cesarean delivery should be accomplished in the operating room; however, preparations must be made for the possibility of delivery in the ICU when transportation cannot be safely or expeditiously accomplished.[75] In the event of cardiopulmonary arrest, a cesarean delivery should be performed at the site of cardiopulmonary resuscitation through a midline abdominal skin incision. Anesthesia is not necessary in this setting.

Search and Eliminate Source of Sepsis

Once the hemodynamic status has been addressed and antibiotic therapy initiated, the next step is to search for and eliminate a potential surgical source of infection. In situations in which there is evidence of infected tissue requiring operative intervention for source control, the appropriate gynecologic or surgical specialists should be involved as the patient is stabilized. Even with appropriate antibiotic therapy, however, the patient may continue to deteriorate unless septic foci (ie, abscess, necrotic tissue) are surgically excised.

Sepsis is characterized by a hyperinflammatory response resulting from microbial infection.[76] Organisms proliferate at the nidus of infection, invade the bloodstream, and release various substances (eg, cytokines, platelet activating factor, complement, kinins, prostaglandins, and leukotrienes) into the blood. These mediators cause most of the clinical manifestations of SIRS including fever, vasodilation, tachycardia, and hypotension.[77] For patients who have endomyometritis after uterine surgery or a septic abortion and who fail to respond despite aggressive antibiotic therapy, it is important to rule out the presence of pelvic or abdominal abscess or microabscesses of the uterus. Imaging of the abdomen and pelvis should be performed to search for abscess (Fig. 6) or intramyometrial gas formation. Surgery should be performed promptly when abnormal findings are identified.

Patients with an abdominal incision or episiotomy, particularly obese women with medical disorders such as diabetes mellitus, nephritic syndrome, and autoimmune disorders requiring immunosuppressive therapy, should be considered at very high

Box 6. Potential Maternal and Perinatal Indications for Delivery With Severe Sepsis or Septic Shock

Maternal
- Intrauterine infection
- Development of disseminated intravascular coagulation
- Hepatic or renal failure
- Compromised cardiopulmonary function by uterine size or peritoneal fluid, or uterine size and peritoneal fluid
  - Compartment syndrome
  - Hydramnios
  - Multifetal gestation
  - Severe adult respiratory distress syndrome or barotrauma
- Cardiopulmonary arrest

Fetal
- Fetal demise
- Gestational age associated with low neonatal morbidity or mortality

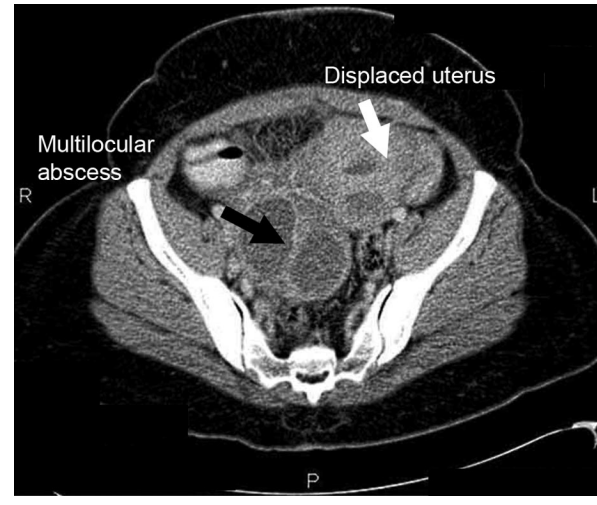

Fig. 6. Postdelivery abdominal computed tomography scan revealing multiloculated abscess. This figure was published in Barton JR, Sibai BM. Management of severe sepsis and septic shock. In: Sibai BM, editor. Management of acute obstetric emergencies. 1st ed. Philadelphia (PA): Saunders, an imprint of Elsevier Inc; 2011. p. 93–100. Copyright © Elsevier, 2011.

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risk for wound complications including abscess formation and necrotizing fasciitis. If these patients have severe sepsis not responding to aggressive therapy, they warrant prompt imaging and a detailed physical examination. The diagnoses of necrotizing fasciitis or necrotizing vulvitis are surgical emergencies.[40,47] Even with appropriate antibiotic therapy, the patient's condition will continue to deteriorate unless the septic foci are eliminated. Management of this condition includes resection of the involved tissue. For necrotizing fasciitis of the abdomen, an incision should be made through the involved tissue down to the fascia with extensive dissection (Fig. 7) and removal of the affected tissue until well-vascularized healthy tissue is reached at the margins. Furthermore, tissue should be submitted for pathology evaluation (Fig. 8) as well as culture and bacterial sensitivities. The incision is packed open and then débrided on a daily basis as necessary. Once recovered, allograft or xenograft skin can be used to cover an open abdominal incision. Finally, it is always advisable to seek surgical consultation to rule out nongynecologic sources of tissue necrosis such as appendiceal or pancreatic abscesses and infarcted bowel.

Maintenance Phase

Once the initial resuscitation phase in the management of severe sepsis or septic shock is complete, the maintenance phase of management should begin. Goals of the maintenance phase should include insulin management for glucose control, consideration of corticosteroids, transfusion of red blood cells as directed by hemoglobin measurement, reassessment of cultures and clinical condition to adjust or narrow antibiotic therapy, thromboembolic prophylaxis, adjustment in ventilator settings in intubated patients to limit long-term lung injury, and assessment of the nutritional status of these patients.

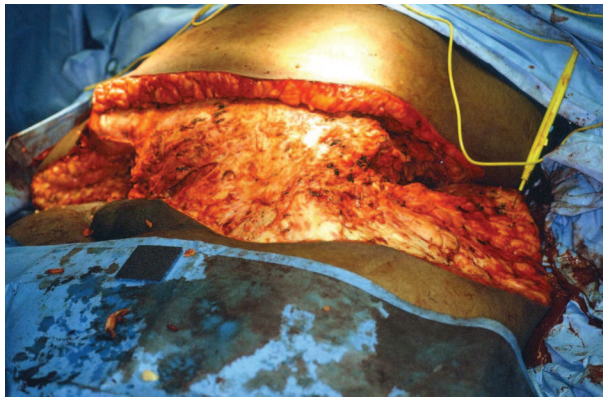

Fig. 7. Extensive abdominal wall and fascia dissection necessitated by postcesarean fasciitis. This figure was published Barton JR, Sibai BM. Management of severe sepsis and septic shock. In: Sibai BM, editor. Management of acute obstetric emergencies. 1st ed. Philadelphia (PA): Saunders, an imprint of Elsevier Inc; 2011. p. 93–100. Copyright © Elsevier, 2011.

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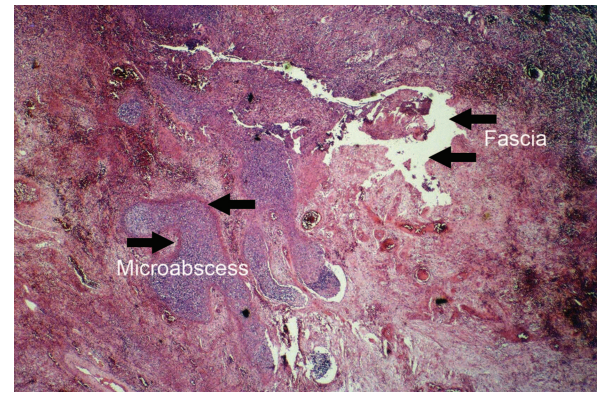

Fig. 8. Pathology sections revealing microabscess in the débridement specimen for the patient in Figure 7. This figure was published in Barton JR, Sibai BM. Management of severe sepsis and septic shock. In: Sibai BM, editor. Management of acute obstetric emergencies. 1st ed. Philadelphia (PA): Saunders, an imprint of Elsevier Inc; 2011. p. 93–100. Copyright © Elsevier, 2011.

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Insulin Therapy

Tight glucose control initially was recommended during the management of severe sepsis[8] on the assumption that normoglycemia would benefit the patient. Subsequent studies in patients with severe sepsis, however, have reported that such intensive glucose control (glucose range 80–110 mg/dL) increased the frequency of hypoglycemia[78,79] and worsened outcomes including increased mortality compared with conventional glucose control.[78] Currently, insulin therapy should be considered when two consecutive blood glucose levels are greater than 180 mg/dL; insulin therapy should be initiated with the target of maintaining blood glucose less than 180 mg/dL.[80] Patients initially should undergo glucose assessment every 1–2 hours, but testing may be spaced to every 4 hours once stable.

Corticosteroids

In clinical practice, the use of corticosteroids has been considered for treating patients with septic shock who require vasopressors despite adequate fluid replacement. In initial studies for patients with septic shock,

hydrocortisone provided earlier reversal of shock and improved survival.[81,82] In a meta-analysis, physiologic steroids (200–300 mg/d hydrocortisone for 7 days in three or four divided doses or by continuous infusion) with subsequent tapering were found to increase survival rate and shock reversal in patients with vasopressor-dependent septic shock.[83] The corticosteroid therapy of septic shock study, however, evaluated the efficacy and safety of low-dose hydrocortisone therapy in a broad population of patients with septic shock. In this study, hydrocortisone did not improve survival or reversal of shock in patients with septic shock either overall or in patients who did not have a response to corticotropin, although hydrocortisone hastened reversal of shock in patients in whom shock was reversed.[84]

Current recommendations would suggest that patients with refractory septic shock poorly responsive to fluid resuscitation and vasopressor therapies receive 50 mg hydrocortisone every 6 hours.[80] The corticosteroids should be tapered, however, once vasopressors are not required as septic shock resolves. Although previously recommended to determine candidacy for corticosteroids, corticotropin stimulation testing is not required.[84]

Transfusion of Red Blood Cells

The pathophysiology of severe sepsis and septic shock results in decreased oxygen delivery and reduced oxygen extraction. As such, early goal-directed therapy protocols initially advocated red blood cell transfusion to achieve a hematocrit of at least 30% if the central venous oxygen saturation was less than 70%.[8] A multicenter randomized controlled trial of transfusion in critical care patients concluded that in the absence of tissue hypoxia, active bleeding, or significant cardiac disease, a restrictive protocol for transfusion of red blood cells should be used to maintain hemoglobin levels above 7 g/dL.[85] Furthermore, transfusion of red blood cells was not warranted for hemoglobin levels above 9 g/dL.[85] These recommendations are also supported by a 2003 review in the Surviving Sepsis Campaign suggesting red blood cell transfusion should be targeted to maintain hemoglobin at 7.0 g/dL or greater.[86] In addition, erythropoietin was not recommended as a specific treatment for sepsis-associated anemia.[86] It is common for patients with severe sepsis to develop a coagulopathy, particularly if their delivery was complicated by excessive hemorrhage. Correction of coagulopathy should be performed if there is continued bleeding or if operative intervention is planned.

Drotrecogin Alfa (Activated)

The recombinant form of human-activated protein C previously was indicated for the reduction of mortality in adult patients with severe sepsis with a high risk of death (Acute Physiology and Chronic Health Evaluation II score 25 or greater). Recently, however, in the PROWESS-SHOCK clinical trial, drotrecogin alfa (activated) (Xigris, Eli Lilly) failed to show a survival benefit.[87] As a result of these findings, the U.S. Food and Drug Administration issued a statement in October 2011 that drotrecogin alfa (activated) should not be started in new patients with sepsis.[88]

Nutrition

Sepsis is characterized by accelerated metabolism and hyperdynamic circulatory changes.[89] In nonobstetric febrile patients, each 1°C increase in temperature increases caloric needs by 10%.[90] As such, these patients require increased nutritional support during their treatment. There is controversy, however, as to the optimal route of nutrition. In a prospective cohort study of ICU admissions by Matsushima et al,[91] patients were assigned to total parenteral nutrition if enteral nutrition was not tolerated by day 3. A multiple logistic regression model demonstrated a nearly fivefold increased risk of catheter-related bloodstream infections with total parenteral nutrition.[91] Recent European Society of Clinical Nutrition and Metabolism guidelines concerning nutrition in a surgical ICU recommend initiation of parenteral nutrition within 24–48 hours for critically ill patients if enteral nutrition is contraindicated or for those who are not expected to be on normal nutrition within 3 days.[92] Of note, enteral feeding may provide several useful physiologic functions including improving bowel blood flow, acting as a barrier to prevent bacterial translocation, decreasing oxidant production, and improving immune function.

PREVENTION

Recent changes in obstetric practice in the United States have led to an increased cesarean delivery rate. Reasons for this increase include medicolegal concerns, lower rate of trial of labor after previous cesarean delivery, and increased maternal habitus. Preoperative preparation and interventions with operative delivery can reduce the likelihood of wound complications and, therefore, septic complications. These include treating infections remote to the surgical site before elective surgery, showering with an antiseptic agent the night before surgery, abstaining from smoking (30 days) before surgery, glycemic

control in diabetics, hair removal around the incision by electric clippers (not by razor), wide antiseptic skin prep before the operative procedure, and antimicrobial prophylaxis.[93] Surgical technique should eliminate dead space and minimize tissue trauma and electrocautery use.

Antimicrobial prophylaxis is recommended before all cesarean deliveries unless the patient is already receiving antibiotics for a separate infection. Single-dose therapy with Gram-positive and Gram-negative bacterial coverage is recommended, with options including 1–2 g cefazolin intravenously or 1–2 g cefotetan intravenously. Antibiotic prophylaxis should be administered up to 60 minutes before skin incision and not at cord clamping as was previously a common practice.[94] This antimicrobial timing has been associated with lower rates of surgical site infection and overall maternal infectious morbidities without an increase in adverse neonatal outcomes.[95,96] Prophylactic antibiotics should be repeated after 4 hours in prolonged surgical cases or those associated with excessive blood loss.

Obese and morbidly obese patients are at increased risk for surgical site infections as a result of decreased tissue antibiotic levels, increased prevalence of diabetes, and difficult exposure, which prolongs operative time and increases tissue trauma with the need for retractors to obtain adequate exposure. Furthermore, obesity is associated with increased tissue hypoxia resulting from the decreased vascularity of the subcutaneous fat as well as having an increased risk for hematoma and seroma formation.[97] Therefore, obese patients should receive a higher dose of preoperative antibiotics, although there is debate as to the weight cutoff (80 kg, 100 kg, or body mass index [calculated as weight (kg)/[height (m)]^2] greater than 30) for the higher dose.

Pregnant women have a disproportionately high risk for serious illness and death from H1N1 influenza A infection[46,98] as well as poor fetal and neonatal outcome.[99] Vaccination is an effective method for preventing influenza infection. The Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices recommends that all women who will be pregnant during the influenza season receive inactivated influenza vaccine at any point in gestation.[100] There is no evidence of increased maternal or fetal risk from influenza immunization[101] and recent data would suggest an actual newborn benefit in reducing newborn laboratory-confirmed influenza virus infection and hospitalization requirement with influenza-like illness.[102]

CONCLUSION

Severe sepsis and septic shock compromise tissue perfusion, which untreated leads to tissue hypoxia, cell death, and end-organ failure. The outcome and survivability in severe sepsis and septic shock in pregnancy are improved with early detection, prompt recognition of the source of infection, and targeted therapy. This can be achieved by formulating a stepwise approach that consists of early provision of time-sensitive interventions such as aggressive hydration, initiation of appropriate broad-spectrum antibiotics, central hemodynamic monitoring, and the involvement of pharmacy, infectious disease specialists, and critical care specialists familiar with the physiologic changes in pregnancy.

The adoption of hospital-wide, guideline-based performance improvement programs targeting severe sepsis has demonstrated mortality benefit.[13] Furthermore, this benefit was observed to increase with level and duration of compliance.[13] The American College of Chest Physicians and the Society of Critical Care Medicine diagnostic criteria for severe sepsis and septic shock to predict morbidity and mortality did not however specifically address the obstetric population. Future research is needed to establish the diagnostic criteria for severe sepsis and septic shock in obstetric patients and potentially propose new values for hemodynamic criteria that may be more clinically appropriate in pregnancy and postpartum. Once these criteria are defined, it becomes imperative to develop protocols and education regarding diagnosis and early goal-directed therapy with resuscitation based on hemodynamic parameters, appropriate antibiotic therapy, and prompt elimination of the source of specific sepsis for an obstetric population.

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