Critical illness requiring admission to an intensive care unit (ICU) is a relatively uncommon complication of pregnancy, accounting for less than 1% of ICU admissions (1). A few illnesses, such as eclampsia, hemorrhage, the HELLP syndrome (hemolysis, elevated liver enzymes, low platelets), amniotic fluid embolism, and tocolytic-induced pulmonary edema, are specific to the pregnant patient and may lead to ICU admission. However, it is slightly more common that nonobstetric diseases occurring in the pregnant patient lead to life-threatening illness.

It is not within the scope of this article to review comprehensively all problems that lead to critical illness in the gravid patient. A recent State-of-the-Art in the Journal provides an excellent overview of this broad topic (2). The management of the critically ill pregnant patient has not changed dramatically in the past decade. Unfortunately, there is a paucity of recent data concerning critically ill obstetric patients. This article concentrates on new information regarding the pregnant patient and recent advances in critical care that will be applied to the pregnant patient even though these studies did not include pregnant patients. These topics include severity of illness and mortality, asthma, pulmonary edema, ventilatory strategies, eicosanoids and nitric oxide, and resuscitation.

SEVERITY OF ILLNESS AND MORTALITY

In a case control study El-Solh and Grant (1) retrospectively compared 93 critically ill pregnant patients with a variety of diagnoses to a similar number of nonpregnant females of the same age admitted to intensive care units. Respiratory illness (31%) and the need for mechanical ventilation (38%) were slightly greater in obstetric patients than in the nonobstetric patients (24 and 24%, respectively). Mortality did not significantly differ (10.8 and 12.5%). Measures of acute severity of illness accurately predicted mortality in both groups. The levels of accuracy of APACHE (Acute Physiology and Chronic Health Evaluation) II, SAPS (Simplified Acute Physiology Score) II, and MPM (Mortality Probability Model) II scores did not differ significantly from each other or between obstetric and nonobstetric patients. Bhagwanjee and coworkers (3) reported a series of ICU admissions of 105 pregnant patients with a diagnosis of eclampsia. They also found the APACHE II score to predict observed mortality (10%). Multiple-organ failure was a strong predictor of mortality. Survivors had fewer failures of organ systems (1.3) compared with those who died (2.9). No patient with failure of at least two organ systems for more than 48 h survived.

These studies support the concept that mortality in critically ill pregnant patients is related to the clinical status of the patient. Pregnancy per se does not increase mortality beyond that expected for the severity of illness. In general, the gravid patient is treated similarly to the nonpregnant patient with the same illness, except for changes to accommodate altered maternal physiology and to ensure fetal safety.

ASTHMA

Asthma is the most common respiratory condition complicating pregnancy and poorly controlled asthma increases maternal and fetal morbidity and mortality (2). In a prospective observational study of 504 pregnant patients with asthma, an 18% incidence of acute asthmatic attacks was observed in patients who were not using inhaled corticosteroids compared with a 4% attack rate in asthmatic patients using inhaled corticosteroids (p < 0.001) (4). Wendel and colleagues (5) studied 58 women hospitalized for 65 acute asthmatic attacks during pregnancy. All were treated with high-dose intravenous methylprednisolone, followed by a tapering oral schedule of this drug at discharge. The patients were randomized to receive continuing therapy with either inhaled corticosteroids and β-agonist or inhaled β-agonist alone. Those receiving inhaled corticosteroids had a readmission rate of 12% whereas the rate was 33% in the group that did not receive inhaled steroids (p < 0.047). Although these studies included a relatively small number of enrollees, they provide strong evidence for aggressive use of inhaled corticosteroids in pregnant patients with asthma to prevent critical illness. There are no data in the literature indicating adverse effects of inhaled corticosteroids on the fetus.

A major concern in treating asthma in pregnant patients is the possibility of fetal toxicity resulting from pharmacologic therapy, especially systemic corticosteroids. Oral corticosteroids were associated with a twofold increase in pre-eclampsia in a study of 824 pregnant women with asthma, but were not associated with an increase in congenital malformations (6). A large, recent case-control study reported a significant increase (odds ratio 6.55) in oral clefts in children born to mothers who received oral corticosteroids during the first trimester of pregnancy (7). However, this study suffers from several deficiencies. First, the histories of first trimester drug exposures were obtained retrospectively from the mothers after delivery and diagnosis of the congenital abnormality, possibly leading to recall bias. Second, only 4 of 1,184 infants with oral clefts had a history of corticosteroid exposure. Third, the period of corticosteroid exposure was highly variable, with one exposure of only two doses of 40 mg of prednisolone. Finally, the logistic regression model in this study did not include confounding variables of maternal illness or degree of smoking. Even if this association of corticosteroids and malformations is confirmed, the incidence of oral clefts in children of women receiving corticosteroids in the first trimester was only 0.4% (7), substantially less than the incidence of untoward perinatal outcome in poorly controlled asthma.
A recent position paper has reviewed use of medications in the treatment of asthma and concludes that severe asthma meets the criteria for use of systemic corticosteroids (8). Short-acting β-agonists have not been associated with congenital malformations or adverse outcomes of pregnancy. Salmeterol is not recommended for routine use in pregnancy because of the absence of human data, but may be considered in compelling circumstances. Concerning newer therapeutic agents, the report does not support the use of the leukotriene modifier zileuton because of adverse effects in animal reproduction studies. Experience with the leukotriene receptor antagonists in animals has been reassuring, but no human data are available. These agents would not be considered for first-line therapy, but possibly may be valuable in individuals in whom these agents have exhibited unique benefit before pregnancy.

PULMONARY EDEMA

The gravid patient undergoes physiological changes in pregnancy that predispose to development of pulmonary edema. Table 1 includes hemodynamic values from 10 stable patients studied both during pregnancy and after delivery (9). The principal alterations occurring in pregnancy are increases in cardiac output and heart rate and decreases in systemic vascular resistance and colloid osmotic pressure. During labor there are large hemodynamic changes, particularly in cardiac output, with values ranging well above and below values listed in Table 1. Even though these individual factors have not correlated with occurrence of pulmonary edema (2), this constellation likely alters fluid balance in the lung and predisposes to development of hydrostatic pulmonary edema. This seems to be the case when pulmonary edema develops after β-adrenergic tocolytic therapy. Most patients are not admitted to a critical care unit and few require mechanical ventilation (10). The majority exhibit marked improvement within 24 h after diuresis. These findings suggest volume overload and a cardiogenic basis for the pulmonary edema. However, this is not always the case. Perry and coworkers (11) described five cases of pulmonary edema after tocolytic therapy that met accepted criteria for acute respiratory distress syndrome (ARDS). In the presence of an associated factor such as simultaneous fetal surgery, classic permeability pulmonary edema has been documented by elevated lung fluid protein content and normal pulmonary capillary wedge pressure (12).

In the presence of usual predisposing causes of ARDS such as infection, aspiration, and hypotension secondary to hemorrhage, pulmonary edema is usually characterized by increased capillary permeability (13). In patients with pre-eclampsia leading to pulmonary edema, there is considerable uncertainty regarding the underlying mechanisms leading to alveolar flooding. Oliguric pre-eclamptic patients may present with elevated systemic vascular resistance but have normal or decreased intravascular volume (14). In addition, patients with elevated systemic vascular resistance may have depressed cardiac function, which produces increased pulmonary capillary wedge pressures.

Uncertainty concerning the mechanism leading to development of pulmonary edema in an obstetric patient hampers decision making in management. As a result, invasive hemodynamic monitoring is advised when alveolar flooding does not respond to initial therapy (14). In addition to pulmonary edema and other usual indications for Swan–Ganz cardiac catheterization, specific obstetric-related indications include pregnancy-induced hypertension complicated by oliguria, the need for rapid antihypertensive therapy, Class 3 or 4 cardiac disease during labor or delivery, anamnestic fluid embolism, and pulmonary hypertension complicating delivery (14).

### TABLE 1. NORMAL CARDIOVASCULAR* AND ARTERIAL BLOOD† GAS VALUES (± SD) FOR WOMEN AT TERM AND POSTPARTUM

<table>
<thead>
<tr>
<th></th>
<th>Antepartum</th>
<th>Postpartum</th>
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<tbody>
<tr>
<td>Cardiac output, L/min</td>
<td>6.2 ± 1.0</td>
<td>4.3 ± 0.9</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>83 ± 10</td>
<td>71 ± 10</td>
</tr>
<tr>
<td>Mean arterial pressure, mm Hg</td>
<td>90 ± 6</td>
<td>86 ± 7</td>
</tr>
<tr>
<td>Systemic vascular resistance, dyn·cm·s⁻⁵</td>
<td>1,210 ± 266</td>
<td>1,530 ± 520</td>
</tr>
<tr>
<td>Colloid osmotic pressure, mm Hg</td>
<td>180 ± 1.5</td>
<td>208 ± 1.0</td>
</tr>
<tr>
<td>Pulmonary capillary wedge pressure, mm Hg</td>
<td>7.5 ± 1.8</td>
<td>6.3 ± 2.1</td>
</tr>
<tr>
<td>pH</td>
<td>7.43 ± 0.027</td>
<td>7.41 ± 0.013</td>
</tr>
<tr>
<td>Pco₂, mm Hg</td>
<td>30.4 ± 2.7</td>
<td>35.3 ± 3.1</td>
</tr>
<tr>
<td>Po₂, mm Hg</td>
<td>102 ± 5</td>
<td>95 ± 7</td>
</tr>
</tbody>
</table>

* Cardiovascular values from Clark and coworkers (9), obtained in left lateral recumbent position at 36–38 wk of gestation and 11–13 wk after delivery.
† Arterial blood gas values from measurements reported in Templeton and Kelman (17), obtained in semirecumbent position with 15° pelvic tilt at 38 wk of gestation and 5 wk after delivery.

### VENTILATORY STRATEGIES

Pregnancy results in a number of physiological changes that must be considered when mechanically ventilating the pregnant patient (15). As pregnancy proceeds, the subcostal angle widens from 68° to 103°, leading to an increased transverse diameter of the chest. This results in an increase in lower chest circumference of 5–7 cm, which compensates for the eventual 4-cm elevation of the diaphragm caused by the enlarging uterus. As a result, total lung capacity decreases only 5% due to a 20% reduction in the residual volume. Vital capacity is not altered. However, the changes in chest configuration produce important changes in static mechanical properties. Lung compliance itself does not change during pregnancy, but compliance of the chest wall decreases approximately 30%, causing a parallel but slightly smaller decrease in total respiratory compliance (16).

Minute ventilation increases by 40% in the first trimester and remains elevated throughout pregnancy. This increase is achieved largely by an increase in tidal volume with little increase in respiratory rate (17). Because minute ventilation increases more than the increased metabolic requirements of pregnancy, arterial Pco₂ falls substantially and the normal gravid individual develops a compensated respiratory alkaloysis (Table 1).

In general, mechanical ventilation for respiratory failure during pregnancy should be approached by using the same techniques employed for the nonpregnant patient, but keeping in mind that arterial blood gas goals differ in the pregnant state (Table 1). However, ARDS presents a particular challenge.

Although there are no studies of utilization of low tidal volumes in treatment of pregnant patients with acute lung injury, the proven efficacy of this mode of ventilation in nonpregnant patients with ARDS provides strong support for its universal use. In the ARDS Network study (18) the delivered tidal volume was based on ideal body weight calculated from patient height. This ideal body weight may not be the same as the ideal body weight of a pregnant patient, but it can be argued that it still should be used to calculate the delivered tidal volume. The goal of low tidal volume therapy is to avoid overdistention of the lung, and because total lung capacity varies little between the pregnant and nonpregnant state, it is reasonable to use this method of determining tidal volume. The ARDS Network study (18) also limited maximum plateau pressures to 30 cm H₂O. It could be argued that the decreased chest wall compliance in the pregnant patient would allow greater pla-
teau pressures without exceeding a reasonable transpulmonary distending pressure. However, as lung compliance falls dramatically in acute lung injury, it becomes the overwhelming determinant of total respiratory compliance. For these reasons, there appears to be little reason to alter the alveolar plateau pressure guideline of the ARDS Network study (18).

The increased ventilation accompanying pregnancy produces respiratory alkalosis and a compensatory metabolic response. It is important to maintain maternal arterial PCO₂ in its usual range of 28–32 mm Hg. Permissive hypercapnia is not an attractive option for ventilating the pregnant patient. Transfer of CO₂ across the placenta is dependent on a PₐCO₂ difference of approximately 10 mm Hg between fetal and maternal umbilical veins. This difference remains fairly constant over a wide range of CO₂ tensions (19). Therefore, maternal hypercapnia quickly results in fetal respiratory acidosis, a factor that limits the use of permissive hypercapnia. Acidosis also shifts the fetal oxygen dissociation curve to the right, limiting the ability to bind oxygen to fetal hemoglobin. The effect of hypercapnia on the fetus potentially could be mitigated by administration of bicarbonate to the mother if bicarbonate ion were transferred into the fetal circulation. Although there are studies that support movement of bicarbonate ion across the human placenta, the data are insufficient to determine whether this rate of transfer is adequate to protect the fetus from the deleterious effects of an elevated maternal arterial PCO₂ (19).

The normal tidal volume in pregnancy (17) is greater than the target value of 6 ml/kg ideal body weight utilized in the ARDS Network study (18). This presents a significant problem in maintaining the normal increased ventilation accompanying pregnancy. The least injurious response is to increase the respiratory rate as long as severe intrinsic positive end-expiratory pressure (PEEP) can be avoided. If this is not sufficient to prevent hypercapnia, an increase in tidal volume should be considered. The goal of low tidal volume ventilation is to avoid overdistention of open alveolar units through exposure to high distending pressures. Therefore, it seems reasonable to increase tidal volume as long as the alveolar plateau pressure does not exceed 30 cm H₂O.

The prone position has been advocated in ARDS to improve gas exchange during mechanical ventilation, but there is no information regarding its use in pregnancy. There also are no data available on the effect of this position on maternal or fetal perfusion.

In many obstetric-related illnesses, delivery of the fetus results in prompt maternal improvement. However, the therapeutic effect of delivery is less certain in the pregnant patient with respiratory compromise. Tomlinson and coworkers (20) reported 10 cases in which delivery was performed in patients requiring mechanical ventilation. Although inspired oxygen concentration could be reduced by 28% within 24 h after delivery, the effect varied widely among patients. Six of the 10 patients either died or required 2 wk of further mechanical ventilation. Thus, imminent delivery does not seem to offer the same benefit in respiratory failure as in some obstetric-related illnesses.

EICOSANOIDS AND NITRIC OXIDE

Eicosanoids have been implicated in the vascular pathophysiology of pre-eclampsia. A number of trials using aspirin as prophylaxis for pre-eclampsia have shown no efficacy. Data from a large multicenter study suggest that women who later developed pre-eclampsia had significantly reduced production of the vasodilator prostaclin many months before clinical onset of the syndrome (21). There was no increase in produc-

tion of the vasoconstrictor thromboxane A₂. The authors postulate that the failure of aspirin as prophylaxis may be explained by the absence of increased thromboxane production in pre-eclampsia.

Nitric oxide (NO) has been implicated in the pathogenesis of pre-eclampsia. A unifying mechanism to explain the spectrum of syndromes ranging from pregnancy-induced hypertension through pre-eclampsia and multisystem organ involvement in the HELLP syndrome has been sought. All appear to involve endothelial dysfunction but no consensus has been reached regarding the underlying pathophysiology.

Because NO has a ubiquitous effect on vascular reactivity, studies have tested the hypothesis that a lack of NO is related to the development of pre-eclampsia. The studies consisted of small numbers of subjects, assayed different biochemical markers, and used control groups at different dates of gestation, but suggest somewhat similar results. Contrary to expectations, published studies of pre-eclamptic women have shown an increase in NO metabolites in peripheral, uteroplacental, and fetoplacental blood samples (22–24). In another study, placental villi and amniotic fluid of pre-eclamptic women showed increased staining for nitric oxide synthase and amniotic fluid contained increased concentrations of NO metabolites (25). The authors postulated that the L-arginine–NO system is up-regulated in pre-eclampsia as compensation to augment uterine blood flow. Thus, the mechanism of vascular pathophysiology in pre-eclampsia appears not to be simply related to lower nitric oxide biosynthesis, and therefore administration of NO would not be a useful therapy for pre-eclampsia.

Nitric oxide has been utilized in the treatment of ARDS in nonpregnant patients, but there is still no consensus on whether inhaled NO improves clinical outcome as defined by oxygen requirements, ventilator days, or mortality. There are only two case reports of NO being used in pregnant women with life-threatening pulmonary hypertension. A patient with HIV-associated pulmonary hypertension was successfully managed for 4 wk by administration of NO at 5 to 20 ppm. Pulmonary vascular resistance decreased; maternal methemoglobin was 1.1% and was undetectable in the newborn (26). In a patient with Eisenmenger’s syndrome, previously refractory hypoxemia improved with inhaled NO. After improvement of oxygenation, the patient delivered a viable infant (27).

There are no data regarding the effect of exogenous NO on the human fetus. Because of rapid, irreversible binding to maternal hemoglobin, NO should not be transported across the placenta. In terms of hemodynamic consequences, there are no data concerning the effect of NO on uterine artery blood flow in humans. No conclusion can be drawn regarding the efficacy of inhaled NO in the pregnant patient.

ACUTE RESUSCITATION

Hypotension in the pregnant patient involves volume resuscitation, vasopressors, and close attention to body position. In the supine position the gravid uterus itself can mechanically compromise venous return. Anecdotal reports in the literature describe return of maternal blood pressure and survival after emergency cesarean section for presumed fatal outcome of attempted maternal resuscitation. With hypotension, placing the mother in the left lateral decubitus position can substantially improve maternal cardiac output and blood pressure as well as correct impaired placental circulation. In cardiopulmonary arrest, resuscitation should follow standard protocols with modification of positioning (28). The recommendation is made to elevate the right hip 15°. Rees and Willis (29) examined the efficacy of resuscitation with the body at various angles of incli-
nation between 0° (supine and the most efficient for standard chest compressions) and 90° (the least efficient for chest compressions but the least impediment to maternal venous return). At an angle of 27° on an inclined board, 80% of the maximal force for chest compression could be delivered. They concluded that this angle provides significant relief of the mechanical obstruction to venous return and maintains sufficient compressive force on the sternum. The Cardiff resuscitation wedge was designed and manufactured as a result of this study. Data concerning the optimal balance of α- and β-adrenergic vasopressor agents in humans are lacking; this underscores the importance of position in the hypotensive pregnant patient.

SUMMARY

The extrapolation of existing studies and principles in the context of a particular clinical situation is necessary when data are not available to reach an evidence-based conclusion. The need for this extrapolation is intensified when the medical decision involves a critically ill pregnant patient in whom altered maternal and fetal physiology must be considered. We have examined advances in critical care and how these may be applied to optimize maternal and fetal outcome.

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References