

than 200 mL/min/m² may also be associated with improved outcome (30).

It was not until 1998 that investigators reported patient outcome when aggressive volume resuscitation (60 mL/kg fluid in the first hour) and goal-directed therapies (goal = CI, 3.3–6.0 L/min/m² and normal pulmonary artery occlusion pressure [PAOP]) were applied to children with septic shock (38). Ceneviva et al (38) reported 50 children with fluid-refractory (≥ 60 mL/kg in the first hour), dopamine-resistant shock. The majority (58%) showed a low CO/high SVR state, and 22% had low CO and low vascular resistance. Hemodynamic states frequently progressed and changed over the first 48 hours. Persistent shock occurred in 33% of the patients. There was a significant decrease in cardiac function over time, requiring addition of inotropes and vasodilators. Although decreasing cardiac function accounted for the majority of patients with persistent shock, some showed a complete change from a low output state to a high output/low SVR state (41–44). Inotropes, vasopressors, and vasodilators were directed to maintain normal CI and SVR in the patients. Mortality from fluid-refractory, dopamine-resistant septic shock in this study (18%) was markedly reduced compared with mortality in the 1985 study (58%) (30), in which aggressive fluid resuscitation could not be accomplished in part because intraosseous vascular access was not yet commonly used and attainment of intravascular access in the resuscitation bay was difficult. More recently investigators in the United Kingdom confirmed these observations using Doppler ultrasound to measure CO (39, 40). They found that previously healthy children with community-acquired sepsis often had a low CO with a higher mortality rate, whereas CO was high and mortality rate was low in septic shock related to catheter-associated blood stream infections (39).

“Neonatal septic shock” can be complicated by the physiologic transition from fetal to neonatal circulation. In utero, 85% of fetal circulation bypasses the lungs through the patent ductus arteriosus (PDA) and foramen ovale. This flow pattern is maintained by supra systemic pulmonary vascular resistance in the prenatal period. At birth, inhalation of oxygen triggers a cascade of biochemical events that ultimately result in reduction in pulmonary vascular resistance and artery pressure and transition from fetal to neonatal circulation with blood flow now being directed through the pulmonary circulation. Closure of the PDA and foramen ovale (that can occur much later) complete this transition. Pulmonary vascular resistance and artery pressures can remain elevated and the ductus arteriosus can remain open for the first 6 weeks of life, whereas the foramen ovale may remain probe patent for years. Sepsis-induced acidosis and hypoxia can increase pulmonary vascular resistance and artery pressure and maintain patency of the ductus arteriosus, resulting in persistent pulmonary hypertension of the newborn (PPHN) and persistent fetal circulation. Neonatal septic shock with PPHN is associated with increased right ventricle work. Despite in utero conditioning, the thickened right ventricle may fail in the presence of systemic pulmonary artery pressures. Decompensated right ventricular failure can be clinically manifested by tricuspid regurgitation

and hepatomegaly. Newborn animal models of Group B streptococcal and endotoxin shock have also documented reduced CO, and increased pulmonary, mesenteric, and SVR (45–48). Therapies directed at reversal of right ventricle failure, through reduction of pulmonary artery pressures, are commonly needed in neonates with fluid-refractory shock and PPHN.

The hemodynamic response in premature, very low birth weight (VLBW) infants with septic shock (< 32-wk gestation, < 1,000 gm) is least understood. Most hemodynamic information is derived only from echocardiographic evaluation, and there are few septic shock studies in this population. Neonatology investigators often fold septic shock patients into “respiratory distress syndrome” and “shock” studies rather than conduct septic shock studies alone. Hence, the available clinical evidence on the hemodynamic response in premature infants for the most part is in babies with respiratory distress syndrome or shock of undescribed etiology. In the first 24 hours after birth during the “transitional phase,” the neonatal heart must rapidly adjust to a high vascular resistance state compared with the low resistance placenta. CO and blood pressure may decrease when vascular resistance is increased (49). However, the literature indicates that premature infants with shock can respond to volume and inotropic therapies with improvements in stroke volume (SV), contractility, and blood pressure (50–63).

Several other developmental considerations influence shock therapy in the premature infant. Relative initial deficiencies in the thyroid and parathyroid hormone axes have been reported and can result in the need for thyroid hormone and/or calcium replacement (64, 65). Hydrocortisone has been examined in this population as well. Since 2002, randomized controlled trials showed that prophylactic use of hydrocortisone on day 1 of life reduced the proportion of patients with hypotension in this population (66), and a 7-day course of hydrocortisone reduced the need for inotropes in VLBW infants with septic shock (67–69). Immature mechanisms of thermogenesis require attention to external warming. Reduced glycogen stores and muscle mass for gluconeogenesis require attention to maintenance of serum glucose concentration. Standard practices in resuscitation of preterm infants in septic shock employ a more graded approach to volume resuscitation and vasopressor therapy compared with resuscitation of term neonates and children. This more cautious approach is a response to anecdotal reports that preterm infants at risk for intraventricular hemorrhage (< 30-wk gestation) can develop hemorrhage after rapid shifts in blood pressure; however, some now question whether long-term neurologic outcomes are related to periventricular leukomalacia (a result of prolonged under perfusion) more than to intraventricular hemorrhage. Another complicating factor in VLBW infants is the persistence of the PDA. This can occur because immature muscle is less able to constrict. The majority of infants with this condition are treated medically with indomethacin, or in some circumstances with surgical ligation. Rapid administration of fluid may further increase left to right shunting through the ductus with resultant pulmonary edema.

One single-center, randomized control trial reported improved outcome with use of daily 6-hour pentoxifylline