Clinical Factors Influencing Blood Pressure in the Neonate

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Objectives
After completing this article, readers should be able to:

1. Describe the association between gestational age, birthweight, and postnatal age and blood pressure in the neonate.
2. Delineate the primary clinical consideration in an infant who has hypotension.
3. Describe the controversy surrounding the relationship between antenatal steroid therapy and neonatal blood pressure.
4. Delineate the aspects of management of respiratory illnesses in the neonate that may be associated with altered blood pressure.
5. List factors that may cause altered blood pressure in the neonate.

Introduction
Few aspects of neonatal care have generated as much controversy as the assessment of blood pressure (BP) and need for treatment of perceived abnormalities of this physiologic variable. Familiarity with clinical situations in which BP may be low should allow anticipation of this common clinical problem and timely intervention when such treatment is necessary (Tables 1 and 2). In this article, we review factors that have been shown to have the greatest effect on BP.

Measuring Blood Pressure
A direct reading from an indwelling arterial catheter represents the “gold standard” for measuring BP in the neonate, and this method should be used whenever possible. Obviously, arterial access may not always be available, and the ability to monitor BP noninvasively using an oscillometric technique represents a major advancement in neonatal care. The correlation between direct and indirect methods generally has been good. Disparities in results have been related to various factors, including inappropriate cuff width-to-arm ratio or problems with the arterial catheter-transducer system, such as air bubbles or clots. In general, indirect determinations are higher than those obtained directly, often by 3 to 5 mm Hg.

Birthweight and Gestational Age
The individual contributions of birthweight and gestational age to BP are difficult to delineate. Several groups of investigators have shown that BP at birth is higher in larger, more mature infants. There is evidence that small-for-gestational age infants have lower BPs than do larger babies of comparable gestational age, which suggests that birthweight per se may be more than a marker for increased maturity.

Early studies involving large numbers of infants who had a wide range of birthweights and gestational ages demonstrated the significance of both of these variables. In a recent report of a large multicenter study conducted by the Philadelphia Neonatal Blood Pressure Study Group, systolic and diastolic blood pressures were significantly correlated with birthweight (Fig. 1) and gestational age (Fig. 2).

Le Flore and associates studied 116 very low-birthweight (VLBW) neonates during the first 72 hours after birth. Following multiple linear regression, both gestational age and birthweight were primary variables predicting mean blood pressure (MBP) during this
period. However, gestational age explained more of the variance in MBP during the first 24 hours, with each additional week of gestation increasing MBP by 1.4 mm Hg. Neonates of 24 to 25 weeks’ gestation had an initial MBP of 27 ± 4 mm Hg versus 39 ± 7 mm Hg for neonates at 32 to 33 weeks’ gestation (P < 0.01) (Fig. 3). In contrast, birthweight explained more of the variance in MBP between 25 hours and 72 hours after birth, with each increase of 100 g associated with an increase in MBP of 1.0 mm Hg. The Joint Working Group of the British Association of Perinatal Medicine has recommended that MBP (in mm Hg) be maintained at or above the gestational age of the infant (in weeks). Further investigation is required to establish the safety and efficacy of this approach.

**Postnatal Age**

As alluded to previously (Fig. 3), MBP increases postnatally in VLBW neonates regardless of gestational age. Zubrow and associates found a similar relationship be-

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**Table 1. Some Risk Factors for Shock in the Newborn**

<table>
<thead>
<tr>
<th>Umbilical Cord Accident</th>
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<tbody>
<tr>
<td>● Avulsion</td>
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<tr>
<td>● Prolapse</td>
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<tr>
<td>● Entanglement</td>
</tr>
<tr>
<td>● Anomalous vessels</td>
</tr>
<tr>
<td>● Vasa previa</td>
</tr>
<tr>
<td>● Velamentous insertion</td>
</tr>
<tr>
<td>Placental Abnormalities</td>
</tr>
<tr>
<td>● Placenta previa</td>
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<tr>
<td>● Placenta abruptio</td>
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<td>● Multilobar</td>
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**Fetal/Neonatal Hemolysis**

- Maternal blood group incompatibility
- Erythrocyte membrane abnormality (eg, hereditary spherocytosis)
- Erythrocyte enzyme abnormality (eg, glucose-6–phosphate dehydrogenase deficiency)

**Fetal/Neonatal Hemorrhage**

- Fetomaternal hemorrhage
- Twin-to-twin transfusion
- Intracranial hemorrhage
- Subgaleal hemorrhage
- Intra-abdominal hemorrhage

**Maternal Factors**

- Infection
- Hypotension
- General anesthesia
- Spinal anesthesia
- Vasoactive drugs

**Other**

- Intrauterine asphyxia
- Infection
- Intrathoracic air leak
- Postoperative
- Positive-pressure ventilation with high airway pressures
- Structural heart defect
- Patient ductus arteriosus
- Arrhythmia

From Faix RG, Pryce CJE (see Suggesting Reading).

**Table 2. Some Causes of Cardiogenic Shock in the Newborn**

**Congenital Heart Disease**

- Hypoplastic left heart syndrome
- Critical aortic stenosis
- Interrupted aortic arch
- Severe aortic coarctation
- Anomalous left coronary artery
- Ebstein anomaly
- Critical pulmonic stenosis
- Arteriovenous fistula
- Hypoplastic right heart syndrome
- Atrioventricular canal

**Myocardial Dysfunction**

- Congenital mycardiopathy
- Myocarditis
- Asphyxia
- Drug intoxication
- Metabolic derangements (eg, glucose, calcium, phosphorous, thyroid)
- Hypertrophic cardiomyopathy
- Systemic infection

**Impaired Venous Return or Cardiac Restriction**

- Pericardial tamponade
- Intrathoracic air leak
- Diaphragmatic hernia
- Postabdominal surgery

**Dysrhythmia**

- Supraventricular tachycardia
- Ventricular tachycardia or fibrillation
- Complete atrioventricular block
- Prolonged Q–T interval syndrome

From Faix RG, Pryce CJE (see Suggesting Reading).
Blood Pressure

Significant hypotension in the neonate can be a reflection of prenatal, intrapartum, or postnatal hemorrhage (Table 1). Fetomaternal, twin-twin, intracranial, subgaleal, and hepatic hemorrhages are the most common types of significant blood loss. Adrenal hemorrhage is a very rare (but reported) cause of severe neonatal hypotension, although the mechanism of subsequent blood pressure instability may be more associated with adrenocortical derangement than significant blood loss. Hemorrhage should be considered in any hypotensive neonate, but it is important to note that the initial physiologic response involves the release of vasoactive substances, such as catecholamines and arginine vasopressin. Hypotension may be a relatively late finding that suggests the presence of acute blood loss. The pre-equilibration hemoglobin and hematocrit values also may be misleading following blood loss.

Antenatal Steroids

Infusion of cortisol into the sheep fetus results in increased arterial pressure. Several reports have suggested that neonatal BP is higher in preterm infants whose mothers received antenatal steroids to hasten fetal lung maturity. This finding would not be unexpected because previous studies have suggested that sick preterm neonates may have relative adrenocorticosteroid insufficiency. Furthermore, successful treatment with hydrocortisone or dexamethasone, administered because of hypotension refractory to conventional therapies, has been documented.

In one study, neonates whose mothers received dexamethasone had higher MBPs during the first 3 days after birth, but this relationship was less clear when adjustment for birthweight was made. After this adjustment, a significant difference in BP was noted only 2 hours following initial treatment with exogenous surfactant. A subsequent study investigated the amount of BP support required by extremely preterm infants (23 to 27 weeks’ gestation) whose mothers did or did not receive antenatal steroids. Infants not exposed to antenatal steroids had lower MBPs from 16 to 48 hours after birth. Furthermore, the use of dopamine was increased in the infants not exposed to antenatal steroids. The reduction in severe intraventricular hemorrhage observed in infants whose mothers received antenatal steroids has been linked to normal BP in those infants. In another study, MBP during the first 24 hours after birth was increased in VLBW infants whose mothers received antenatal steroids, and volume expansion and vasopressor support were decreased in those infants.

Conversely, LeFlore and associates reported no differences in MBPs among 116 VLBW neonates whose mothers did or did not receive antenatal steroids, and similar results were obtained in another study. Other investigators have reported a tendency for higher mean BP in infants weighing at least 1,000 g whose mothers received antenatal steroids but a tendency for lower MBP in infants weighing less than 1,000 g who were exposed to antenatal steroids. Leviton and colleagues found no difference in the incidence of lowest MBP less than 30 mm Hg in infants whose mothers did or did not receive a complete course of antenatal glucocorticoid prophylaxis.

Obviously, further investigation is required to determine the relationship between antenatal steroids and BP. Perhaps in the subset of preterm infants who truly have relative adrenal insufficiency, antenatal steroids may enhance neonatal cardiovascular stability and raise BP, while antenatal steroids have little or no effect on BP in those who have adequate adrenal function.
Route of Delivery

The effect of route of delivery on BP in the neonate has been studied extensively. Several studies in term neonates have indicated that BP in vaginally delivered infants is higher than in those delivered by cesarean section. In general, these studies have attributed the higher BP in the former group to increased catecholamine concentrations and cord blood arginine vasopressin and adrenocorticotropic hormone levels. However, among VLBW infants, blood pressures were similar in infants delivered vaginally and those delivered by cesarean section. Likewise, in the study by Zubrow and associates, which included 106 infants of 32 weeks’ gestational age or younger, stepwise multiple linear regression analysis did not identify route of delivery as a significant determinant of BP variation. Breast delivery has been associated with BP in the lower range of normal. The volume of placental transfusion (as well as postnatal transfusion) also may affect BP.

Asphyxia

The classic studies of Dawes in newborn monkeys demonstrated that BP initially rises with ongoing asphyxia, but after 5 minutes, it decreases progressively. As emphasized by the American Academy of Pediatrics/American Heart Association Committee on Neonatal Resuscitation, many infants who have birth depression and possibly some degree of hypotension respond to effective positive-pressure ventilation and do not require specific measures to raise BP (see accompanying article on treatment of hypotension).

Apnea

Circulatory changes resulting from apnea in the neonate have been summarized by Miller and Martin. The initial decrease in heart rate is accompanied by a rise in pulse pressure, usually due to an increase in systolic pressure. These events presumably result from increased filling volume associated with bradycardia, which leads to enhanced stroke volume in accordance with Starling’s law. As the severity of apnea and bradycardia increases, BP may decrease, along with a fall in cerebral blood flow velocity. Thus, during prolonged apnea, cerebral perfusion may decrease significantly, placing the infant at risk for brain injury.

Pulmonary Disease and Treatment

Infants who have severe respiratory distress syndrome (RDS) may have lower BPs than those observed in healthy preterm neonates or infants who have less severe RDS. An association in infants who have RDS between marked fluctuations in arterial BP and fluctuating cerebral blood-flow velocity has been demonstrated. Also, an association has been reported between acute hypocarbia and marked systemic hypotension.

Three aspects of respiratory management in preterm neonates have been shown to affect BP: 1) use of increased airway pressures, given either by constant positive airway pressure (CPAP) or intermittent mandatory ventilation; 2) suctioning of the airway, occasionally accompanied by a fall in diastolic pressure; and 3) instillation of an exogenous surfactant preparation into the airway. Although a number of studies in animals and humans have shown no effect of positive end-expiratory pressure or CPAP on BP, Kluckow and Evans observed a highly significant negative influence of mean airway pressure on MBP in preterm neonates requiring mechanical ventilation. BP fluctuations during mechanical ventilation may be decreased through the use of various methods of synchronized mechanical ventilation.

Perlman and Volpe measured arterial BP, cerebral blood-flow velocity, and intracranial pressure in 35 intubated preterm neonates undergoing routine suctioning. MBP increased during suctioning in all but one patient, and these investigators concluded that the observed increases in cerebral blood-flow velocity and intracranial pressure were directly related to the increased blood pressure. Perry and colleagues reported an association between systolic BP above a “stability boundary” and increased periventricular-intraventricular hemorrhage, with BP elevations related temporally to suctioning. In addition to suctioning, BP response to various care procedures, including chest auscultation and physiotherapy, mouth rinsing, diaper changing, and nasogastric feeding, have been studied, and in general, BP responses were biphasic, with a decrease in BP followed by a greater and longer lasting increase.

Numerous investigators have studied the physiologic effects of surfactant instillation in neonates, and differences in these reports may be due to dosing or technique of administration. In most studies, any effects on BP were transient. There may be greater hemodynamic effects associated with natural surfactant preparations, perhaps related to their generally more rapid pulmonary effects compared with artificial surfactant preparations.

Patent Ductus Arteriosus

Studies of patent ductus arteriosus (PDA) in animals and preterm human neonates generally have shown significant decreases in diastolic BP. In one study, investigators noted that a diastolic BP of less than 28 mm Hg sug-
gested the presence of PDA, although it is apparent from numerous studies that many normal VLBW neonates actually have mean BPs lower than 28 mm Hg.

Among infants whose birthweights were 1,000 to 1,500 g, Evans and Moorcraft found similar BPs in the PDA and nonPDA groups. However, in those whose birthweights were less than 1,000 g, mean systolic and diastolic BPs were lower in infants who had PDA compared with those who did not. Furthermore, these hemodynamic effects could be demonstrated well before the PDA became clinically apparent. These authors cautioned against the use of volume expanders or inotopic agents in this population because these treatments might be counterproductive if the cause of the hypotension is a hemodynamically significant but clinically silent PDA. Furthermore, volume expansion appears to be a risk factor for the development of symptomatic PDA in VLBW neonates. It is apparent that problems with low BP related to PDA, especially diastolic BP, may result in inadequate perfusion of vital organs because of the “vascular steal” phenomenon. Optimum management of this clinical problem, of course, is directed at closure of the PDA rather than increasing the BP by other means.

Sepsis
Neonatal sepsis is a common problem that can be devastating in both preterm and term neonates. The complicated pathophysiology of neonatal sepsis involves activation or release of numerous inflammatory and vasoactive substances, and hypotension can be a relatively late finding. The resulting effect on the cardiovascular system can be vasoconstriction, as is seen frequently in term and postterm septic neonates who have pulmonary hypertension or peripheral vasodilation with accompanying cardiomyopathy resulting in profound systemic hypotension (see accompanying article on treatment of hypotension). Necrotizing enterocolitis, which often accompanies sepsis, continues to be a common problem in the neonatal intensive care unit, and neonates who have moderate-to-severe disease very frequently are hypotensive.

Other
Maternal smoking may be associated with increases in both systolic and diastolic BP in the neonate, and a direct relationship between neonatal BP and the number of cigarettes smoked has been shown. This effect may persist for at least 12 months. Although maternal hypertension may be a factor associated with higher neonatal BP, this is not reported consistently. Cocaine exposure in utero has been shown to be associated with increased BP on the first day after birth in term neonates, and increased circulating catecholamine concentrations have been demonstrated. Mean arterial pressure was unchanged, but arterial pressure variability was decreased with both pancuronium and pethidine (meperidine). Fentanyl and midazolam may cause hypotension in neonates. Numerous studies have demonstrated that BP may increase and decrease with pneumothorax. Seizure activity may have variable effects on blood pressure. Increased neonatal BP has been documented in infants who have chronic lung disease and receive dexamethasone therapy.

Summary
The smallest, least mature infants have lower BPs than infants who are larger and more mature. The effect of antenatal steroids, given to the mother when preterm delivery is anticipated, is controversial. Maternal smoking and route of delivery are perinatal factors that can influence neonatal BP. Sepsis and hemorrhage are associated with significant derangements in BP and always must be considered in a hypotensive neonate. PDA may be associated with a significant decrease in diastolic BP.

Suggested Reading
Dawes G. Fetal and Neonatal Physiology. Chicago, Ill: Yearbook Medical Publishers; 1968
Moise AA, Warden ME, Kozinetz CA, Gest AL, Welty SE, Hansen TN. Antenatal steroids are associated with less need for blood


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**NeoReviews Quiz**

1. The blood pressure (BP) in a newborn is influenced by several maternal and neonatal factors. Of the following, the most accurate statement regarding neonatal BP is that:

   A. A small-for-gestational age neonate has higher a BP than an appropriately grown infant of the same gestational age.
   
   B. Each additional week of gestational age increases the mean BP by 1.0 mm Hg.
   
   C. Each 100-g increment of birthweight increases the mean BP by 1.4 mm Hg.
   
   D. Gestational age contributes more to the variance in BP than birthweight during the first postnatal week.
   
   E. The correlation between direct and indirect methods of BP measurement is poor.

2. Prenatal, intrapartum, or postnatal hemorrhage may cause low BP in a newborn. Of the following, the least common cause of hemorrhage associated with low BP in a neonate is:

   A. Adrenal.
   
   B. Fetomaternal.
   
   C. Hepatic.
   
   D. Intracranial.
   
   E. Subgaleal.

3. Antenatal maternal factors or postnatal neonatal treatments may cause high BP in a newborn. Of the following, the most likely cause of neonatal hypertension is:

   A. Maternal corticosteroid treatment.
   
   B. Maternal hypertension.
   
   C. Maternal smoking.
   
   D. Surfactant instillation.
   
   E. Vaginal delivery.