Left ventricular performance and contractility before and after volume infusion: a comparative study of preterm and full-term newborn lambs

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ABSTRACT We studied left ventricular performance and contractility after volume loading in lambs at 122 days (group I, n = 9) and 139 days gestational age (group II, n = 9) and in 8-day-old full-term lambs (group III, n = 7). All were mechanically ventilated; each preterm lamb was treated with surfactant to stabilize pulmonary function and the ductus arteriosus was occluded with an inflated catheter balloon. Cineangiograms, left ventricular and vascular pressures, and the isovolumetric index of contractility, first derivative of left ventricular pressure (dP/dt), were recorded before and after three successive whole blood volume infusions of 10 ml/kg (total 30 ml/kg). The left ventricular end-diastolic volume per kilogram and stroke volume per kilogram increased significantly in all groups after volume infusion; these measurements and heart rate and systemic vascular resistance did not differ significantly between the groups either before or after the infusions. The left ventricular peak dP/dt did not change significantly within the groups during the volume infusions. The left ventricular stroke work was greatest in full-term animals and increased significantly in all groups after volume infusion. Thus, the left ventricles of the preterm and full-term lambs had quantitatively similar Frank-Starling responses and there was no increase in contractility during the infusions of whole blood. However, the left ventricle of the full-term lamb is capable of generating greater stroke work than that of the preterm lamb. These findings may contribute to the understanding of developmental aspects of postnatal circulatory adaptation.

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IT HAS BEEN suggested that the left ventricle of the premature infant may be less capable than the mature left ventricle of adjusting to transitional circulatory changes required postnatally, such as increasing volume and resistance work.1,2 These conclusions followed from ultrastructural observations and from developmental studies of myocardial contraction in isolated muscle preparations, and from comparative studies of left ventricular performance in the intact fetus and full-term newborn lamb.1-8 Until recently developmental studies of postnatal left ventricular performance were not possible in newly born preterm animals, because prematurity was associated with a rapid deterioration of pulmonary function and metabolic status.9,10

Now, however, acceptable pulmonary function can be maintained with the combined use of surfactant treatment and mechanical ventilation.10 The purpose of this study was to characterize developmental aspects of left ventricle pump performance and contractility in surfactant-treated preterm lambs and in full-term lambs under conditions simulating those encountered in the neonatal intensive care setting.

Material and methods

We studied the hemodynamic responses to volume infusions in three groups of preterm and full-term lambs. Group I lambs (n = 9) were 122 ± 2 (SD) days gestational age, group II lambs (n = 9) were 139 ± 2 days gestational age, and group III (n = 7) consisted of 8 ± 3 day old spontaneously delivered full-term lambs. The preterm lambs were delivered by cesarean section of date-bred Western mixed-breed ewes. The ewes (groups I and II) were premedicated with intramuscular injections of ketamine (800 mg) and atropine sulfate (3 mg), and surgery was performed under spinal anesthesia. The head and neck of each lamb were exposed through an anterior midline abdominal incision, and an appropriately sized endotracheal tube was secured in the
trachea by tracheotomy under local anesthesia. Preterm lambs at 122 days gestational age cannot be successfully ventilated without surfactant treatment, whereas preterm lambs at 139 days gestational age do not require surfactant treatment for adequate ventilation. Therefore, before delivery and initiation of breathing, the group I lambs (122 days gest age) were treated by tracheal instillation with 15 ml of 0.45M NaCl containing natural sheep surfactant in suspension (50 mg lipid per kg). The surfactant was isolated from lung lavage from adult ewes. Each preterm lamb was then delivered and cord blood was drawn for measurements of pH and arterial blood gases. The cord was clamped and cut, and each lamb was then ventilated with a pressure-limited infant ventilator (Sechrist Industries) at initial settings of 30 breaths/min, a positive end-expiratory pressure of 2 cm H2O, a peak inspiratory pressure of 28 cm H2O, and an inspiratory time of 1 sec. A No. 5F catheter was passed via an umbilical artery to the distal thoracic aorta, and each lamb was paralyzed with intravenous pancuronium bromide (0.1 mg/kg). Rectal temperature was maintained at 38° to 39°C with a heating pad and heat lamps. Blood losses were replaced with equivalent volumes of freshly collected anticoagulated and filtered maternal blood. Peak inspiratory pressures, rates, and inspired oxygen concentrations were changed to maintain arterial blood gas values in the range Po2 50 to 80 mm Hg, Pco2 30 to 45 mm Hg, and pH 7.35 to 7.45. Arterial blood gases and pH were measured at 20 to 30 min intervals with a Radiometer blood gas analyzer.

Group III lambs were brought to the laboratory where they were premedicated with intravenous atropine, 0.01 mg/kg, and ketamine, 0.5 mg/kg. Each lamb was intubated with a 5.5 mm endotracheal tube by direct laryngoscopy. The lambs were paralyzed with pancuronium bromide (0.1 mg/kg) and ventilatory settings were adjusted to maintain blood gases and pH within similar and acceptable ranges for study of cardiovascular performance.

**Catheter placement.** The lambs were catheterized under local anesthesia through small external cutdowns while fluoroscopy and pressure monitoring were performed (figure 1). The tracheotomy incision was extended laterally; two fluid-filled catheters were passed via the right external jugular vein into the right atrium (No. 5F argyl catheter) and into the main pulmonary artery (No. 5 flow-directed balloon angiography catheter). A No. 5F transducer-tipped catheter (Millar Instruments, Inc.) was advanced retrogradely from the right carotid artery to the left ventricle. A No. 4F flow-directed balloon angiographic catheter was passed via the umbilical vein (femoral vein in group III) through the foramen ovale and advanced to the left ventricle. A No. 5F polyvinyl catheter was advanced from the umbilical artery (femoral artery in group III) to the descending thoracic aorta.

In group I and II lambs the catheter in the pulmonary artery was advanced into the ductal lumen and the balloon was then inflated to occlude the ductus arteriosus. The catheter was secured and occlusion during the duration of the protocol was confirmed by pressure monitoring and fluoroscopy. The ductus arteriosus was occluded in preterm lambs to eliminate the variable influence of left-to-right ductal shunting on ventilricular performance. Using this method, we have occluded the ductus arteriosus for several hours in preterm lambs.

**Measurements and calculations.** The cardiovascular pressures were continuously monitored and recorded with a multi-channel photographic recorder (Hewlett-Packard). Transducers were calibrated with a mercury manometer and referred to zero position at the midthoracic level (lateral decubitus position) before each series of measurements. The transducer-tipped catheter (left ventricular) was similarly calibrated and was peri-

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**FIGURE 1.** Image obtained at catheterization (left) and single-frame of cine left ventriculogram (right) from the closed-chest preterm and full-term lamb preparation. Venous catheters are advanced to the right atrium (RA) and to the pulmonary artery. A contrast-filled inflated catheter balloon (arrow) occludes the lumen of the ductus arteriosus (upper left). A flexible No. 4F balloon angiography catheter (angio cath; Edwards, Santa Ana, CA) and transducer-tipped catheter (dp/dt) have been introduced into the left ventricle (LV).
odically matched to the pressure tracing obtained in vivo from the fluid-filled left ventricular angiographic catheter. The left ventricular end-diastolic and systolic pressures before and during angiography were measured from recordings originating from the transducer-tipped catheter. The rate of rise of first derivative of the left ventricular isovolumetric pressure (dP/dt) and the peak rate of rise (peak dP/dt), were calculated with a Hewlett-Packard derivative preamplifier. The left ventricular end-diastolic pressure was measured at the onset of isovolumetric pressure (systolic rise of dP/dt).

Left ventriculograms were obtained from lambs in the left lateral decubitus position to provide a maximum projection of the left ventricular major axis. Diluted contrast (0.75 ml/kg Renografin 60%, Squibb) was injected through the left ventricular angiography catheter and cineangiograms were recorded on 16 mm film at a rate of 60 frames/sec. Left ventricular volumes were calculated by the single-plane area-length method. The projected frames of two to three initial cardiac cycles were drawn by two observers and the mean left ventricular end-diastolic and end-systolic volumes, stroke volumes, and ejection fractions were calculated. The left ventricular volumes were normalized to body weight (kg) and the calculated left ventricular volumes were then corrected with the use of regression equations derived from comparisons of volumes calculated from projected 16 mm cine frames of preterm and full-term lamb left ventricular casts with their corresponding displacement volumes. We have described a 12% mean difference between such calculated volumes and their actual water displacement values. Stroke work index per kilogram was calculated by the standard equation with the stroke volume normalized for body weight.

Protocol.* To evaluate left ventricular performance and contractility, we obtained measurements before and after successive volume infusions. In preliminary studies 0.9% NaCl was employed for the volume infusions; however, the left ventricular end-diastolic pressures generally did not increase, and arterial blood gas values uniformly deteriorated in preterm lambs. Consequently, we chose to use maternal blood. Additional preliminary studies indicated that pulmonary, metabolic, and hemodynamic values deteriorated after a fourth (10 ml/kg) whole blood infusion; therefore, we chose to perform and analyze the responses observed after a maximum of three successive infusions.

After intubation and catheterization the arterial blood gases and pH were monitored and the lambs were allowed to stabilize for 20 to 30 min. Baseline data, including blood hematocrit, arterial blood gases, pH, cardiovascular pressures, and left ventricular cineangiograms, were obtained and, after 10 minutes stabilization, the volume infusions were administered as follows: Ten milliliters per kilogram of freshly collected, warmed (38° to 39°C), anticoagulated maternal blood was delivered into the right atrial catheter by an electronically controlled pump over a 2 min period. Two minutes were allowed for stabilization, and cardiovascular pressures and left ventricular cineangiograms were again recorded. The lambs were allowed to stabilize for 5 to 6 min; a blood sample was obtained for assessment of ventilatory status, and the volume infusion and measurements were repeated. The completed protocol consisted of three volume infusions of whole blood (total 30 ml/kg) and the hemodynamic measurements, which were repeated at approximately 10 min intervals.

Statistics. Comparisons between data obtained from each of the three groups before and after the volume infusions were performed with the use of analysis of variance (ANOVA). The comparisons of data obtained within each group before and after volume infusion were performed with paired t tests (two-tailed). The relationship between animal weight and left ventricular end-diastolic volume was examined by linear regression analysis. The p values for the various statistics (e.g., ANOVA) were adjusted for multiple comparisons of group means with the Bonferroni or Student-Newman-Keuls test. A significant difference was considered to exist when p < .05. All data are expressed as mean ± SD.

Results

The birth weights of the lambs were as follows: group I, 2.2 ± 0.6 kg; group II, 3.5 ± 0.5 kg; group III, 4.5 ± 1.6 kg (table 1). The baseline preinfusion measurements were obtained when the preterm animals were at similar postnatal ages: group I, 87 ± 21 min; group II, 89 ± 26 min. The preinfusion arterial pH and blood gases were maintained in acceptable ranges in the preterm and full-term lambs. The baseline hematocrit and arterial pH/blood gas values were similar to those previously described in comparable preterm and full-term lambs. Thus, the lambs maintained acceptable ventilatory and metabolic status during catheterization, recovery, and study periods.

Baseline hemodynamic measurements. The mean resting heart rate was higher in the full-term lambs, but was not significantly greater than in preterm lambs (table 2). The resting heart rates were comparable to values previously described in unanesthetized full-term lambs and in similar preterm lamb preparations. Left ventricular end-diastolic volume was directly related to animal weight (figure 2): left ventricular end-diastolic volume and stroke volume normalized to body weight (kg) did not differ significantly between the groups (table 2 and figure 3). The left ventricular stroke work, however, increased progressively in each group (figure 4). The angiographically estimated cardiac output was highest in the group III lambs, and the higher cardiac outputs were related to the combined increments of the mean heart rates and left ventricular end-diastolic volumes, since ejection fractions were very similar in all groups (table 2). The left ventricular peak dP/dt was significantly greater in group III lambs (table 2). Pulmonary vascular resistance was significantly less in full-term animals; systemic vascular resistance did not differ significantly between the groups.

Volume infusion studies. The hematocrits, arterial blood gases, and pH did not change significantly after the three sequential volume infusions (table 1), indicating that stable and acceptable ventilatory and metabolic conditions were maintained during the course of the protocol.

The data and statistical analyses comparing the

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*This protocol was reviewed and carried out in accordance with the standards of the American Physiological Society.
groups before and after the infusions are shown in figures 2 to 4. The heart rates did not change significantly during or after the volume infusions (figure 3). Left ventricular end-diastolic pressures increased significantly in all groups and were significantly greater in group III (17 ± 3 mm Hg) than in group II (13 ± 2 mm Hg) or in group I (11 ± 2 mm Hg) (p < .01) (figure 4). Although mean systemic pressures increased in all groups, systemic vascular resistance did not change in groups II or III, and decreased significantly in group I (figure 3).

The left ventricular end-diastolic and stroke volumes increased significantly within each group after the infusions, but when expressed per kilogram of body weight the increase in volumes did not differ significantly between the groups (figure 3). Left ventricular stroke work increased in all groups and was significantly greater in group III than in II or I (figure 4). The left ventricular peak dP/dt values did not change significantly during the infusions (table 2).

Discussion
This study compares the hemodynamic responses of the left ventricles of newly born preterm lambs (0.8 to 0.9 gestation) with the responses of 1-week-old full-term lambs. The catheterization procedures required only small cutdowns, minimum sedation, and local anesthesia; the experimental manipulations (volume infusion, cineangiocardiology) caused little discomfort or physiologic disturbance of the animal preparation. In addition, the use of natural sheep surfactant provided reasonable and stable pulmonary function. Thus, we were able to study developmental cardiovascular physiology in preterm lambs under relatively atraumatic conditions and under circumstances simulating those that newborn infants may encounter in the neonatal intensive care unit. We recognize that a rigorous characterization of left ventricular pump performance would require control of the variables heart rate, preload, contractility, and afterload, but the purpose of this study was to evaluate developmentally related hemodynamic responses of the intact circulation. Consequently, control of these variables was neither feasible nor desirable.

Resting mean heart rates in preterm and full-term lambs were comparable to the cardiac rates described in fetal lambs instrumented for long periods and newborn preterm and full-term lambs of similar gestational ages. Although mean heart rate did not differ within the groups, the generally greater rate in full-term animals might lead to smaller resting left ventricular end-diastolic volumes in these lambs. In this study left ventricular end-diastolic volume normalized to body weight did not differ significantly in preterm vs term animals. However, angiographically estimated left ventricular end-diastolic volumes were directly

<table>
<thead>
<tr>
<th>Group</th>
<th>Gestational age (days)</th>
<th>Weight (kg)</th>
<th>Hematocrit (%) Before first infusion</th>
<th>Hematocrit (%) After final infusion</th>
<th>pH Before first infusion</th>
<th>pH After final infusion</th>
<th>Po2 (mm Hg) Before first infusion</th>
<th>Po2 (mm Hg) After final infusion</th>
<th>Pco2 (mm Hg) Before first infusion</th>
<th>Pco2 (mm Hg) After final infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (n = 9)</td>
<td>122±2</td>
<td>2.2±0.6</td>
<td>36±5</td>
<td>34±6</td>
<td>7.38±0.07</td>
<td>7.34±0.04</td>
<td>55±12</td>
<td>75±25</td>
<td>28±4</td>
<td>34±4</td>
</tr>
<tr>
<td>II (n = 9)</td>
<td>139±2</td>
<td>3.5±0.5</td>
<td>32±3</td>
<td>33±2</td>
<td>7.34±0.03</td>
<td>7.34±0.06</td>
<td>60±9</td>
<td>82±21</td>
<td>36±6</td>
<td>34±6</td>
</tr>
<tr>
<td>III (n = 7)</td>
<td>8±3</td>
<td>4.5±1.6</td>
<td>28±6</td>
<td>31±5</td>
<td>7.38±0.05</td>
<td>7.35±0.03</td>
<td>70±7</td>
<td>70±10</td>
<td>36±2</td>
<td>39±5</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

*Postnatal age.

**TABLE 2**
Baseline hemodynamic data

<table>
<thead>
<tr>
<th>Group</th>
<th>Heart rate (bpm)</th>
<th>LVEDV (ml/kg)</th>
<th>EF%</th>
<th>LVO (ml/kg/min)</th>
<th>R syst (mm Hg/ml/kg/min)</th>
<th>RPA (mm Hg/ml/kg/min)</th>
<th>Peak dP/dt (mm Hg/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>196±21</td>
<td>1.6±0.2</td>
<td>66±5</td>
<td>210±33</td>
<td>0.23±0.06</td>
<td>0.12±0.01</td>
<td>2069±504</td>
</tr>
<tr>
<td>II</td>
<td>181±28</td>
<td>2.3±0.6</td>
<td>62±4</td>
<td>253±45</td>
<td>0.24±0.06</td>
<td>0.12±0.03</td>
<td>2654±46^</td>
</tr>
<tr>
<td>III</td>
<td>232±64</td>
<td>2.1±0.5</td>
<td>62±8</td>
<td>303±71*</td>
<td>0.31±0.08</td>
<td>0.07±0.02^</td>
<td>4368±1156^</td>
</tr>
</tbody>
</table>

*a II > I (p < .05); *II > I (p < .05); *III > I (p < .01); *III > II (p < .05); *III < I (p < .01). EF(%) = ejection fraction; LVO = left ventricular output; RPA = pulmonary vascular resistance; R syst = systemic vascular resistance.
correlated with body weight during gestation. Kirkpatrick et al.⁴ and Anderson et al.⁵⁺¹⁹ noted progressively increasing left ventricular dimensions (seminior axis) in fetal sheep in which ultrasonic crystals had been implanted for an extended period, and these increases were independent of cardiac rate. Others also noted a correlation between left ventricular end-diastolic volume and body weight in full-term newborn lambs during the first months of life.²⁰

Angiographically estimated cardiac output per kilogram body weight was significantly greater in group III animals. The greater cardiac output of these lambs was primarily related to the generally greater mean heart rate and end-diastolic volume, since ejection fraction increased minimally at term. Similarly, Anderson et al.¹⁹ did not observe changes in extent of left ventricular shortening in their fetal and full-term lambs instrumented for long periods. Although cineangiocardiography overestimates stroke volume and calculated left ventricular output, the mean cardiac output in our full-term lambs (303 ml/kg/min) was near the lower limit of previously reported values in unanesthetized full-term newborn lambs (265 to 425 ml/kg/min).⁶ ¹⁸ ²¹⁻²⁴ Klopstein and Rudolph⁶ reported substantially greater cardiac output and a remarkable postnatal increase of left ventricular stroke volume in chronically instrumented, spontaneously breathing, unanesthetized 1-week-old full-term lambs at heart rates similar to those in this study.⁶ However, it has been observed that postnatal body oxygen consumption and cardiac output are closely related to environmental temperature and spontaneous respiratory activity.² ²⁴ In view of the good resting left ventricular function in our lambs, it is possible that the low “normal” cardiac output we observed in group III was related to the control of ambient temperature and the use of muscle relaxants and assisted ventilation.

Volume infusion (Frank-Starling response) has been widely used to characterize developmental aspects of left ventricular performance in fetal and full-term newborn lambs.³ ⁴ ⁶ ¹⁷ We have observed intact Frank-Starling responses in preterm and full-term newly born lambs. Volume infusion caused quantitatively similar increases over resting left ventricular end-diastolic volumes and stroke volumes in the three groups, since ejection fractions did not change. Heart rates were stable during the volume infusions. The hemodynamic responses of fetal lambs have been variably reported. Although Heymann and Rudolph³ did not observe a left ventricular Frank-Starling response, Kirkpatrick et al.⁴ and Anderson et al.⁵ demonstrated a positive response in the intact fetus at approximately 0.8 gestation. Similarly, variable responses were observed in full-term lambs.⁵ ¹⁷ Romero and Friedman¹⁷ did not observe a Frank-Starling response after the infusion of saline. However, it is noteworthy that these investiga-

FIGURE 3. Hemodynamic responses of group I and II preterm and group III full-term lambs before and after (arrows) the three sequential 10 ml/kg whole blood volume infusions. Left ventricular end-diastolic (LVED) and stroke volumes increased significantly within each group (*: p < .001), but there were no significant differences between the groups with respect to left ventricular volumes, ejection fractions, heart rates, or systemic vascular resistances before or after the infusions (in preterm lambs systemic resistance decreased after infusions).
LABORATORY INVESTIGATION—VENTRICULAR PERFORMANCE

FIGURE 4. Left ventricular stroke work vs left ventricular end-diastolic pressure before and after volume infusions in preterm and full-term lambs (the sequential infusions begin at the arrow). The left ventricular stroke work increased significantly (*; p < .001) within each group after volume infusions. Baseline and postinfusion stroke work of full-term animals was greater than in preterm animals (††, III > I, p < .001; *, III > II, p < .01).

Tors noted a rise in systemic vascular resistance during volume infusion in their preparations and suggested that the increase may have blunted the Frank-Starling response.

We did not observe such increases in systemic resistance during the infusion of whole blood in our lambs. Furthermore, we noted in preliminary studies that saline infusion did not cause a substantial rise of left ventricular filling pressures and was associated with deterioration with respect to blood gases in several preterm lambs. It is possible that saline may extravasate from “leaky” capillaries, leading to a rise in systemic vascular resistance and inadequate expansion of vascular volume. The use of whole maternal blood may have more effectively expanded blood volume and increased myocardial oxygen availability in our preparation and these factors may account for the demonstrable Frank-Starling responses we observed. Klopfenstein and Rudolph demonstrated a Frank-Starling response in 1-week-old full-term lambs, but the response was reduced in magnitude when compared with that in 6-week-old lambs. However, they suggested that the apparently reduced response to left ventricular volume loading may have been related to the higher basal cardiac output requirements of the newborn animal. Furthermore, at comparable heart rates, the greater cardiac output they observed in 1-week-old lambs was presumably related to a larger left ventricular end-diastolic volume and/or ejection fraction than observed in this or prior studies. Thus, it is possible that at ambient temperature the spontaneously breathing newborn lamb uses much of its “inherent” left ventricular Frank-Starling response. Our studies indicate that preterm and full-term newborn lambs have similar left ventricular volume loading responses; however, they may have similar limitations as well.

Although characterization of the Frank-Starling performance did not demonstrate substantial differences between left ventricular performance in preterm and full-term lambs, we did observe that both before and after volume infusion the left ventricle of the full-term lamb accomplished greater stroke work than that of the preterm lamb. The increase was primarily related to the greater systemic arterial pressure in the full-term animal. Other studies have demonstrated that isolated myocardium from the newborn animal at term developed greater tension than that from the preterm animal. Similarly, it is apparent that at comparable filling volume and systemic arterial resistance, the left ventricle of the intact full-term newborn lamb is capable of developing greater force than the left ventricle of the preterm lamb.

The peak dP/dt has been widely applied to describe contractility of the left ventricle, but this isovolumetric index of contractility is also influenced by alterations in heart rate and preload. The baseline peak dP/dt data were similar to those previously described in preterm and full-term lambs. and Park et al. suggested from studies of isolated myocardium and intact fetal sheep that increased contractility...
was associated with myocardial maturation. However, the greater left ventricular peak dP/dt we measured in group III lambs may have been related to the higher cardiac rate and developed left ventricular pressure as well as to differences in contractility.26 The newborn myocardium may be more sensitive to circulating catecholamines.1, 2, 27, 29-32 Immediately after birth there was a marked and sustained increase in circulating catecholamines that was of greatest magnitude in the preterm lamb.29, 30 The left ventricular contractility increased dramatically after birth in full-term newborn lambs. On the other hand, the left ventricle had less "reserve" contractility.5, 18, 19, 27 However, the left ventricular responses to volume infusion or naturally occurring “volume overload” may differ from those induced by pharmacologic interventions. The measure of contractility, peak dP/dt, generally increases during volume infusion.26 The increase may be caused by increasing end-diastolic volume (independent of alteration of contractility), and/or by volume-induced augmentation of catecholamine release and left ventricular contractility.26, 33 Fujisawa et al.33 demonstrated increasing catecholamine secretion and increased contractility in the adult canine immediately after opening of an experimental arteriovenous fistula. In contrast, we have observed in both the preterm and full-term lamb that left ventricular contractility, as represented by peak dP/dt, does not increase during volume infusion. Similarly, in preterm lambs with patent ductus arteriosus, left-to-right ductal shunting, and an associated increase in left ventricular volumes there was no increased left ventricular peak dP/dt.11 Thus, it is possible that the left ventricles of both preterm and full-term lambs function near their “maximum” level of contractility augmented by the postnatal catecholamine surge and that they are unable to increase contractility further in face of volume load.

This study emphasizes comparative hemodynamics in the intact circulation without standardizing variables that may influence left ventricular performance. Under these experimental circumstances the left ventricle of the preterm lamb possessed considerable reserve volume pumping capacity (Frank-Starling response), which was essentially equivalent to that in the full-term animal at comparable heart rate, preload, and afterload. On the other hand, the left ventricle of the full-term lamb was able to generate greater force or stroke work. The latter finding corresponds well with the known rapid multiplication of contractile units and accelerated increase in left ventricular mass toward the end of gestation.34-36 These observations may be related to characteristics the left ventricle should possess for successful transition from fetal to postnatal life.2 We have demonstrated that both the preterm and term left ventricle appear well adapted to assume the increased volume work that is required to provide oxygen delivery for greater postnatal metabolic demands.2, 22 Consequently, the left ventricle functions at a relatively high level of performance and this may exhaust much of the “inherent” reserve volume pumping capacity of the left ventricle of the newborn.2, 6, 22 Finally, the maturing left ventricle is capable of generating greater force as the end of gestation approaches and therefore becomes well adapted to impending postnatal alterations in vascular impedance as well.11, 20 These considerations may be relevant to the intensive care of the neonate with cardiovascular distress associated with pathologic alterations in left ventricular performance, vascular volume, or systemic vascular resistance.

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