SUMMARY Left cardiac dimensions and an index of left ventricular performance, the percent shortening of the internal diameter (%SID) of the left ventricle, were evaluated in premature infants who were asymptomatic, others with pulmonary disease and others with patent ductus arteriosus (PDA). In contrast to controls, left atrial and/or left ventricular end-diastolic dimensions were increased in all infants with clinical criteria of significant PDA. Postoperative dimensions decreased significantly.

Percent SID values for normal premature infants (m = 33.5%; sd = 3.5%) and those with pulmonary disease alone did not differ significantly. In those with clinical criteria of PDA, who were subsequently found to have echocardiographic evidence of left cardiac enlargement, values for %SID were increased. As expected %SID values for individual patients represented a wider range of left ventricular function and/or afterload than for controls. Upon spontaneous or surgical closure of the PDA, %SID returned to normal.

A PDA which is associated with left cardiac enlargement exhibits increased %SID, whereas decreasing %SID in the presence of increased dimensions suggests deteriorating myocardial performance. Echocardiography provides valuable insight into the cardiac status of these infants and may contribute to their medical and/or surgical management.

NONINVASIVE EVALUATION of cardiac performance in the critically ill premature infant with PDA and pulmonary disease is difficult and frequently inconclusive. Echocardiographic measurements of left atrial1-3 and left ventricular4 dimensions have provided an index of degree of left-to-right shunting through the PDA in premature without pulmonary disease.

It would be of considerable additional interest to determine an index of myocardial contractility in these premature infants because echocardiographic determinations of the diameter of the left ventricle at its minor axis4-7 and the calculation of the extent or percent of shortening at this internal diameter8-12 compare favorably with values obtained by left ventriculography. A diminished percent of shortening of this internal diameter (%SID) correlates well with abnormal myocardial contractility and clinical cardiac decompensation.10-12 The purpose of this study was to determine the %SID of the left ventricle and left cardiac dimensions in premature infants with PDA. We determined the left cardiac dimensions and %SID in asymptomatic premature infants, in premature infants with pulmonary disease alone, and in premature infants with PDA with or without pulmonary disease.

Clinical Material and Methods

Two hundred and twenty-nine serial echocardiographic studies were obtained in 66 premature infants. Gestation, determined on the basis of maturation index,* ranged from 26-36 weeks. Weights at the time of evaluation ranged from 620-2300 grams. Infants excessively small for dates (length and/or birth weight less than the 10th percentile for gestational age16) were not included. During the hospital course, the infants were placed in one or more of three groups according to the following clinical, roentgenographic, and laboratory criteria.

Group 1, asymptomatic infants, consisted of 25 infants without clinical signs of respiratory distress17, 18 or patent ductus arteriosus.19-22 At the time of study, no infant required supplemental oxygen; hemoglobin was greater than 10 g%, and hematocrit was greater than 30%. At the time of study weights ranged from 720-2300 grams with a mean of 1526 grams; chest roentgenograms were normal or showed minimal evidence of pulmonary disease.

Group 2, infants with pulmonary disease, consisted of 17 premature infants with clinical respiratory distress17, 18 and laboratory and roentgenographic evidence of moderate to severe pulmonary disease at the time of echocardiographic study. Weights ranged from 810-2300 grams with a mean of 1511 grams. Nine infants had a roentgenographic diagnosis of respiratory distress syndrome (hyaline membrane disease), four had diffuse atelectasis or aeration disturbance, three had bronchopulmonary dysplasia, and one had transient tachypnea of the newborn. All infants required an increased concentration of ambient oxygen. Assisted ventilation was necessary in five while continuous positive alveolar pressure was required in two. The presence of a PDA at the time of study was excluded by clinical means,19-22 and infants with signs of a significant PDA during the subsequent hospital course were excluded from this group.

Group 3, infants with patent ductus arteriosus in the presence or absence of pulmonary disease, consisted of 40 infants. All had signs of PDA19-22 including active precordial impulse, bounding peripheral pulses, and systolic or continuous murmur at the upper left sternal border and infraclavicular area at the time of echocardiographic study.

Thirty-three group 3 infants had signs of respiratory distress17, 18 and laboratory and roentgenographic evidence of moderate to severe pulmonary disease at the time of study, while seven were clinically asymptomatic and had essentially normal roentgenograms or minimal evidence of pulmonary disease prior to the clinical detection of the PDA. At the

*In this institution adapted from references 13-16.
time of study, roentgenograms of those with pulmonary disease were suggestive of respiratory distress syndrome in seventeen. In sixteen additional infants roentgenograms initially suggestive of respiratory distress syndrome progressed to diffuse aeration disturbance, white-out or bronchopulmonary dysplasia. Twenty-nine infants required assisted ventilation by respirator or were receiving continuous positive alveolar pressure at the time of study.

In four of 40 infants with PDA, including two without pulmonary disease, the PDA did not appear to contribute to the clinical course. Twelve infants (three without pulmonary disease) had persistent signs of PDA and were treated medically for suspected congestive heart failure (i.e., digitalization 30–40 μg/kg/24 hr, fluid and sodium restriction appropriate for age; maintenance of hematocrit > 40%; parenteral furosemide 1 mg/kg initially and as required for signs of fluid retention). At the time of study, weights ranged from 700–1910 grams with a mean of 1278 grams. Twenty-four infants (two without pulmonary disease) had a large PDA based on clinical criteria. That is, all had persistent signs of PDA (as described above), and all ultimately required surgical ligation of the PDA for suspected refractory congestive heart failure (i.e., failure to demonstrate improvement of, or progressive deterioration of, pulmonary and/or cardiovascular status for 24–72 hours following institution of therapy for cardiac failure). At the time of study, weights ranged from 620–1800 grams with a mean of 1115 grams.

Echocardiograms were obtained with a Hoffrel ultrasonoscope Model 101 which produced a peak intensity of 5W/cm² and an Aerotech 7.5 MHz 3 mm active diameter transducer. Studies were generally performed within 15 minutes in the isolette with minimal distress to the infant. Left atrial and left ventricular dimensions were measured as previously described. To ensure consistency of technique and optimal recordings of left atrial and ventricular dimensions, multiple sweeps or scans (from the apex to the aortic root) were obtained with the transducer in the 3rd or 4th left interpace as previously described (fig. 1). Further, both septal surfaces as well as portions of the mitral valve leaflets were included in the echograms when measurements were made. Percent shortening of the internal diameter (%SID) of the left ventricle was derived from an average of 3 to 5 ventricular complexes. Although in many cases echograms were obtained more frequently, serial studies in groups 1 and 2 infants were analyzed only if there was a one week interval and a 100 gram weight increment between studies. When possible, group 3 infants were studied serially prior to and during treatment for suspected congestive heart failure and following spontaneous or surgical closure of the PDA. Postoperative examinations were performed in twelve infants within 24 hours and at least within 72 hours in the remainder.

Results

1. Dimensions

A. Groups 1 and 2

Left ventricular end-diastolic (LVED) and end-systolic (LVES), and left atrial (LAD) dimensions were determined serially for 25 group 1 and 17 group 2 infants. The correlations between weight and LVED, LVES and LAD were strong for both groups (table 1A). No significant difference for weight (table 1A) and dimensions (table 1B, 1C) was found between groups 1 and 2.

A significant difference was found between the weights of group 1 and group 3 medically and surgically treated infants (table 1A). Therefore, analysis of covariance using weight as a covariate was employed to test for significant differences of left cardiac dimensions, %SID and heart rate between the groups. This analysis demonstrated significant differences between the groups; the P values for adjusted means of the variables (dimensions, %SID, heart rate) of group 1 controls versus groups 2 and 3 are shown in table 1C. The regressions for weight versus LAD and LVED and 95% prediction limits for a future individual are shown in figures 3 and 4. In the subsequent discussion the 95% limits served as control or normal values. The left atrial and ventricular dimensions did not exceed these limits in any control infant. However, in one infant with pulmonary disease the left atrial dimension was minimally increased while in another the LVED was minimally increased.

![Figure 1](http://circ.ahajournals.org/). Preoperative (left) and postoperative (right) echocardiograms of the left atrium in a premature infant with PDA. The transducer has been scanned sequentially from the left ventricle to the left ventricular outflow tract and left atrium (L.A). Preoperative left atrial dimension (LAD) was enlarged; postoperatively it returned to normal. A = aortic root; LAW = left atrial wall; RV = right ventricular outflow tract.
B. Group 3 (40 premature infants)

Left ventricular dimensions and LAD values were compared to those of controls (table IC). In four (two without pulmonary disease), the PDA did not appear to contribute to the clinical course, and the dimensions were normal (figs. 3 and 4).

Medically Treated (12 infants). In contrast to controls, eight infants had enlarged LAD prior to treatment. During treatment, dimensions became abnormal in three and returned to normal in four. The LVED was enlarged in six infants prior to therapy and with treatment was enlarged in nine. Two infants were treated for suspected congestive

**Figure 2.** Preoperative echograms of the left ventricle in two prematures with PDA. The infant at left had large dimensions and normal left ventricular %SID. The infant at right had increased dimension and increased %SID. LVE = left ventricular endocardium; LVES = left ventricular end-systolic dimension; LVES = left ventricular end-systolic volume; LS = left septal surface; MV = mitral valve; %SID = percent shortening of the internal diameter; RV = right ventricle.

**Table 1. Summary of Statistical Analysis**

**A. Correlation (r): Weight versus**

<table>
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<th>Group</th>
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**B. LAD versus LVED**

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**C. LAD versus LVES**

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**D. Preoperative versus postoperative studies**

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Abbriviations: adj grp mean = adjusted group mean; HR = heart rate; LAD = left atrial dimension; LVED = left ventricular end-diastolic dimension; LVES = left ventricular end-systolic dimension; M = group mean; Med = medically treated prior to therapy; %SID = percent shortening internal diameter left ventricle; se = standard error; Surg = surgically treated prior to therapy.
heart failure in spite of normal dimensions. LAD and LVED of medically treated infants were significantly greater than those of controls (table 1C); LVES did not differ significantly. In nine studies following spontaneous closure of the PDA, the LAD returned to normal in seven, and LVED returned to normal in eight.

**Surgically Treated (24 infants).** All infants who underwent ligation of the PDA had increased LAD preoperatively, and 21 had increased LVED preoperatively (figs. 3, 4). The LAD became abnormal during medical treatment in four and became normal in two. The LVED increased in four and decreased in one. LAD, LVED and LVES in surgically treated infants were significantly greater than those of controls (table 1C). In addition, prior to surgery the adjusted left atrial dimensions for surgically treated infants were significantly greater than those of medically treated infants ($P < 0.001$); LVED also tended to be significantly greater ($P < 0.07$). Postoperative dimensions decreased significantly (table 1D). LAD was normal in 18, and LVED was normal in 17 of 21 infants in whom studies were available within the first 72 hours postoperatively (figs. 3, 4) in spite of persistent pulmonary disease with roentgenographic abnormalities and the need for assisted ventilation in the majority of infants.

**II. Percent SID Values**

Percent SID was determined serially for 25 group 1 and 17 group 2 infants. No significant correlation was found for %SID and weight (table 1A) and heart rate did not correlate with weight (table 1A) or differ significantly between the

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**Figure 3.** Preoperative and postoperative left atrial dimensions. The regression (solid line) for weight versus left atrial dimension of controls and the 95% prediction limits for a future individual (dashed lines) are represented. Preoperative dimensions were significantly enlarged. Postoperative dimensions decreased significantly and returned to the normal range in the majority. (Anticongestive measures included the use of digitalis, diuretics and appropriate sodium/fluid restriction.)

**Figure 4.** Preoperative and postoperative left ventricular dimension. Normal control values are represented by the regression line (solid) and prediction limits (dashed). Preoperative left ventricular diastolic dimensions were significantly enlarged. Postoperative dimensions decreased significantly and returned to normal in the majority. (Anticongestive measures involved the use of digitalis, diuretics and appropriate sodium/fluid restriction.)
groups (table 1B, 1C). The t-test yielded no significant difference for %SID values between groups 1 and 2 (table 1C). Group 1 mean %SID ± 2 SD (33.5 ± 7.0%) served as the control value (fig. 5). The range of values was less than the mean ± 2 SD, and thus no control was abnormal as defined by the mean ± 2 SD. Percent SID of group 2 infants did not differ significantly from controls (table 1C).

Medically Treated (12 infants). Prior to therapy, %SID was greater than the upper limit for controls in six of eight with left cardiac enlargement and in three with normal dimensions. The %SID values differed significantly from controls (table 1C). During medical treatment, values increased in one and decreased in four. Upon spontaneous closure of the PDA, SID values returned to the normal range (fig. 5) and did not differ significantly from controls.

Surgically Treated (24 infants). Prior to ductal ligation, %SID was significantly greater than the upper limit for controls (fig. 5) in 17 of 24 infants (table 1C). The other seven had %SID in the normal range and underwent surgical ligation. The normal %SID in these seven patients suggested decreasing cardiac performance. Following medical therapy, values increased in three and fell in two; following ligation, %SID decreased significantly (table 1C, fig. 5) and did not differ significantly from controls.

Discussion

An increased incidence of PDA has been demonstrated in preemies with pulmonary disease.29, 34, 38-40 Because congestive cardiac failure may lead to increased mortality and morbidity in these infants,29, 34 evaluation of the premature infant with patent ductus arteriosus and pulmonary disease is an important problem in the neonatal intensive care unit. Clinical detection of PDA may be difficult since the presence of a cardiac murmur and bounding peripheral pulses varies with alterations of cardiac output, systemic and pulmonary vascular resistances and ductal tone.18, 20 A recent study has noted the absence of a cardiac murmur in a significant number of preemies with respiratory distress syndrome and angiographically demonstrated patent ductus arteriosus.29 In addition, assessment of the degree of shunting and the signs of congestive heart failure are difficult to interpret in the presence of significant pulmonary disease. Roentgenographic29, 34 and electrocardiographic29-31 studies are also of limited value particularly in the presence of pulmonary disease. In this study, the roentgenographic diagnosis of cardiomegaly and/or pulmonary edema was considered in only seven of 34 infants with PDA and pulmonary disease (five of 22 in whom large caliber PDA was observed intraoperatively), whereas the diagnosis was more apparent in five of seven preemies without pulmonary disease.

Accurate measurements of cardiac chamber sizes and indices of cardiac performance may be readily obtained by echocardiographic evaluation of critically ill premature infants. Several methods have been utilized to assess the significance of PDA in the premature and include: 1) the determination of absolute left atrial and ventricular dimensions,2 and 2) the ratio of left atrial to aortic dimensions (LA/AO ratio).3, 5 We have continued to rely upon absolute left atrial and ventricular dimensions. All infants with a large caliber PDA at operation had significantly increased LAD and/or LVED (table 1C, figs. 3, 4). Of the surgically treated infants with left atrial enlargement, 81% had increased LVED prior to and 87% had increased LVED during medical treatment for congestive heart failure. Increased LVED in the presence of normal LAD was observed initially in only one infant. It is possible that left atrial enlargement was seen more frequently because the left atrium is more compliant than the left ventricle, and volume overload may cause left atrial dilatation prior to left ventricular dilatation. Dimensions in surgically treated infants were significantly greater than those of medically treated infants. Postoperatively (figs. 3, 4) dimensions decreased significantly (table 1D) and returned to normal despite persistent moderate to severe pulmonary disease and the need for assisted ventilation in the majority. Return to normal occurred in nine of 12 studied within the first 24 hours postoperatively. Values for cardiac dimensions in medically treated infants were significantly greater than those of controls (table 1C). In contrast to surgically treated infants, the enlargement of chambers frequently persisted or increased in spite of therapy for cardiac failure and clinical improvement. Dimensions ultimately returned to normal upon spontaneous closure of the PDA.

In contrast to infants with PDA, no control infant had increased (i.e., false positive) values for left cardiac dimensions. It is appreciated that a clinically undetected PDA may have been present in some group 2 infants with normal dimensions (i.e., a false negative value). However, a large flow PDA seemed unlikely in these infants in view of the consistent and normal serial dimensions in these infants in the symptomatic and asymptomatic state, the relatively uncomplicated course with rapid resolution of pulmonary disease, and the absence of congestive heart failure during the hospital course. Subsequent to ligation of the PDA, the majority of premature infants had persistent severe pulmonary disease, and dimensions did not differ significantly from controls. Thus, the 95% prediction limit for dimensions appears
to be a useful index for discriminating the infant with a large left-to-right shunt through the PDA from the normal infant and those with pulmonary disease.

The major goal of this study was to determine the left ventricular %SID in prematures with clinical criteria of PDA as further evidenced by echographic left cardiac enlargement. The left ventricular %SID is an easily obtained and reliable index of cardiac contractility. Although we recognize that mean velocity of circumferential fiber shortening is a useful index of myocardial contractility, we did not evaluate this parameter because we could not accurately and readily measure left ventricular ejection time in the critically ill premature infant. We have demonstrated significantly greater values of %SID prior to treatment in medically and surgically managed infants with PDA and left cardiac enlargement than were determined in controls or those with pulmonary disease (table 1C, fig. 5). As would be expected for a large group with varying levels of systemic and pulmonary vascular resistances and varying states of myocardial contractility, a wider range of values for %SID was observed in infants with PDA. Seventy-five percent of medically treated group 3 infants and 71% of our babies with a large PDA at operation had a %SID greater than normal. Values for %SID in the normal range and decreasing serial %SID values were observed in a minority (29%) of prematures with a large PDA at operation. Following spontaneous or surgical closure of the PDA, %SID values decreased significantly (table 1D) and did not differ significantly from controls (t = 1.53, fig. 5).

Several factors limit the use of the %SID of the left ventricle as an index of myocardial contractility in the premature infant with PDA. Clinical criteria of congestive heart failure are subjective in these infants. Simultaneous hemodynamic and echocardiographic correlations have not been available in prematures as in adults. Several authors have suggested that improved shortening and velocity relationships could occur in the presence of decreased left ventricular afterload, associated with aortic and mitral insufficiency. More recently, others41-43 have demonstrated augmented shortening and velocity values in direct response to a controlled decrease of left ventricular afterload.

It is of interest that we and others4 have observed exaggerated left ventricular shortening and velocity values in premature infants with large left-to-right shunts and left ventricular volume overload. Left ventricular afterload may be inordinately decreased in the premature infant with a large PDA because the diameter of the ductus may be relatively large44, 45 (appeared equivalent to that of the descending aorta in the majority of our infants), the pulmonary arteriolar musculature is poorly developed46, 47 and vasmotor and myocardial responses to circulating catecholamines may be blunted.48, 49 It has been suggested that the myocardium of the newborn and the premature may be less capable of adapting to increased workload particularly in the presence of hypoxia, hypercapnia and acidosis.50 Thus the increased %SID of the left ventricle we have observed in prematures with a large PDA may be explained by augmented left ventricular unloading into a low resistance circuit offered by the combined systemic and pulmonary vascular beds.

In prematures a relationship between decreased afterload and increased %SID may serve as an index of significant left-to-right shunt through the PDA. However, a single value of %SID is of limited use for the assessment of left ventricular contractility in the presence of decreased left ventricular afterload. Nevertheless, serial evaluations of the left ventricular %SID may provide indications of relative changes in myocardial contractility or afterload. In the premature, a large PDA is associated with left atrial and ventricular enlargement and in the majority of infants an increased %SID (table 2). In the presence of increased shunting through the PDA associated with a decreasing pulmonary vascular resistance (i.e., diminished left ventricular afterload) and increasing left cardiac dimensions, a decrease of %SID on serial determinations may suggest a relative deterioration of left ventricular contractility (table 2).

Thus, echocardiography may provide valuable insight into the hemodynamic and clinical status of critically ill premature infants with patent ductus arteriosus in the presence or absence of pulmonary disease. Because of the trends toward surgical treatment of the PDA in prematures, it is essential that objective criteria be established for the assessment of the cardiovascular status of these infants. This study has correlated echographic findings with currently accepted clinical criteria of significant patent ductus arteriosus. In view of the limitations of clinical assessment of babies with PDA and pulmonary disease, it is evident that there is a need to correlate echocardiographic and hemodynamic data in future studies.

Hopefully, as our experience broadens, serial echocardiographic assessment may provide objective criteria with which to identify noninvasively those infants with PDA who would benefit most from medical and/or surgical intervention.

References

3. Sahn DJ, Vaucher Y, Williams DE, Friedman WF: Echo distinction of left to right shunts from non-structural heart disease in infancy. (abstr) Circulation 50 (suppl II): III-16, 1974

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<tr>
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<td>Large</td>
<td>Increased</td>
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PDA—decreasing cardiac performance

PDA—closing

Table 2. Summary of Echocardiographic Analysis of Premature Infants with PDA
Left ventricular performance in the critically ill premature infant with patent ductus arteriosus and pulmonary disease.
B Baylen, R A Meyer, J Korfhagen, G Benzing, 3rd, M E Bubb and S Kaplan

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