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## DEVELOPMENTAL CHANGES IN VENTRICULAR FUNCTION IN THE CHICK EMBRYO

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How ventricular function changes during embryonic development is unknown. We correlated measures of ventricular physiology with ventricular dry weight and myocyte myofibril and mitochondrial volume in stage 18 (3 day), 21 (3½ day), 24 (4 day), 27 (5 day) and 29 (6 day) chick embryos. In ovo measurements of ventricular pressure and dorsal aortic blood velocity were made with a servo null system and 20 MHz pulsed-Doppler respectively.  $dP/dt$  and  $dV/dt$  were electronically derived. Percent cell volume of mitochondria and myofibrils were determined from electron micrographs of the ventricular wall. From stage 18 to 29, ventricular weight increased from  $28 \pm 2 \mu\text{g}$  ( $\bar{x} \pm \text{SEM}$ ) to  $140 \pm 6 \mu\text{g}$  while embryo weight increased from  $1.02 \pm 0.05 \text{ mg}$  to  $15.36 \pm 0.30 \text{ mg}$ . Ventricular systolic and end-diastolic pressure, and  $dP/dt$  increased from  $1.31 \pm 0.05 \text{ mmHg}$ ,  $.23 \pm 0.03 \text{ mmHg}$  and  $23 \pm 1 \text{ mmHg/s}$  respectively to  $3.45 \pm 1.10 \text{ mmHg}$ ,  $.82 \pm 0.03 \text{ mmHg/s}$  and  $80 \pm 4 \text{ mmHg/s}$ . Dorsal aortic  $dV/dt$  increased from  $878 \pm 17 \text{ mm/s}^2$  to  $2076 \pm 65 \text{ mm/s}^2$ . Relative myofibril volume increased from 17% at stage 18 to 24% at stage 27 but decreased to 18% at stage 29, while mitochondria volume remained constant at 11%. With development, heart:embryo weight ratio and function measures indexed for myocardial weight or myofibril percent decreased as much as 50%. We speculate that the decrease in indexed function may be due to changes in energy utilization, available energy, or geometric shape of the developing heart.

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## CARDIOPULMONARY EFFECTS OF A PATENT DUCTUS ARTERIOSUS.

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The premature newborn's response to increasing degrees of Lc→Rt PDA shunt is unknown. In 14 fetal lambs at 128d gestation (term 147d), we infiltrated the ductus with formalin and placed a mechanical occluder about it so that its patency could be regulated. 3d later the lamb was delivered, given sheep surfactant, paralyzed and mechanically ventilated. Microsphere measurements of left ventricular output (LVO) and its distribution were made prior to and 1.25 h after a change in ductus patency. Twenty four changes from open→closed or closed→open were assigned randomly from 3 to 7 h after delivery. Lambs with ductus shunts < 50% LVO (38%) had a significant increase in LVO (167 vs. 268 ml/kg/min:closed vs. open) with no change in effective systemic blood flow or BP. There was a significant increase in coronary flow but no change in flow to the kidneys, GI tract, brain, or carcass (ml/100 gm/min). Although lambs with shunts > 50% LVO (65%) had a significant increase in LVO (164 vs. 300 ml/kg/min), there was a significant decrease in effective systemic blood flow and BP. There were significant decreases in flow to the kidneys, GI tract, brain and carcass. Coronary flow was unchanged but there was a decrease in subendocardial flow. There was no change in HR or pulmonary compliance at either degree of shunt. Preterm lambs are capable of compensating for moderate degrees of PDA shunt by increasing preload and increasing stroke volume; higher degrees of shunt significantly decrease organ blood flow.

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## NONINVASIVE ESTIMATION OF PULMONARY ARTERY (PA) PRESSURE IN CHILDREN BY DOPPLER ULTRASONOGRAPHY.

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Noninvasive means for PA pressure assessment has been sought without a reliable method found. Doppler interrogation of PA flow offers the potential for an easily performed method of estimating PA pressure from changes in velocity patterns. 34 children, ages 1 day-23 yrs (mean 5.3 yrs) with a variety of cardiac abnormalities, underwent simultaneous PA Doppler study and PA pressure measurement during the course of routine cardiac catheterization. 14 had peak systolic pressures greater than 40 torr. Data was collected by an on-line computer with analysis being performed by computer. Time from onset of ejection to peak velocity (TPV) was measured and compared to that of a separate group of 33 nl pts, similarly studied. As TPV varied inversely with heart rate (HR) in nls, TPV was divided by predicted TPV (TPVN) as determined by linear regression equation ( $TPVN = 182 - 0.79 \times \text{HR}$ ) derived from nl pt data. The ratio of TPV/TPVN was HR independent. TPV/TPVN was linearly related to peak PA pressure ( $r = 0.88$ ,  $p < .01$ ), and less well to PA mean ( $r = 0.85$ ) and PA diastolic pressure ( $r = 0.77$ ). From nl pt data TPV/TPVN ratios < 0.74 were considered abnormal. No pt with a PA peak pressure < 40 torr had an abnormal ratio (100% specific). 13 of 14 with PA pressures > 40 torr had ratios < 0.74 (93% sensitive). Thus TPV/TPVN is an easily measured noninvasive parameter which is a highly sensitive and specific predictor of pts with significant PA systolic hypertension.

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## SYSTOLIC LEFT VENTRICULAR AND AORTIC BLOOD FLOW RESPONSE TO INCREASING SYSTEMIC VASCULAR RESISTANCE

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Classical indices of myocardial performance may be insensitive to changes in myocardial reserve when native afterload is reduced. The objective of this study was to examine the response of left ventricular and regional aortic blood flow to changes in systemic vascular resistance (SVR) in a canine model using combined gated pulsed doppler echocardiography (GPDE) and a non-imaging cardiac probe (NICP). SVR was augmented by continuous methoxamine infusion and calculated by standard thermodilution techniques in 5 animals (3-5kg). Aortic blood flow was evaluated by GPDE interrogation of the thoracic aorta. Systolic aortic blood flow was described by the mean velocity and the frequency time integral partitioned into the first and latter two-thirds of systole. The left ventricular ejection rate and stroke volume were measured simultaneously by NICP. Increasing SVR resulted in a pansystolic reduction in the mean ejection rate of the left ventricle and mean systolic aortic flow velocity. A normal reciprocal relationship was present for the first and latter two-thirds of left ventricular and aortic systolic blood flow as measured by percent change of stroke volume. This baseline relationship persisted with increasing SVR. In conclusion, combined GPDE and NICP can provide an effective means to noninvasively evaluate left ventricular performance and regional aortic blood flow changes with augmentation of afterload.

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## GATED PULSED DOPPLER ASSESSMENT OF SIMPLE COARCTATION OF THE AORTA IN PEDIATRIC PATIENTS.

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Pulsatile flow dynamics are altered distal to an area of obstruction. To investigate the effects of simple coarctation of the aorta (CAo) on descending aortic blood flow patterns, doppler interrogation of the thoracoabdominal aorta was performed in 12 infants with CAo less than 18 months of age, and 15 age matched controls. All patients with CAo demonstrated continuation of high forward flow throughout the cardiac cycle with prolongation of both acceleration and deceleration phases. Indexing the ratio of acceleration and deceleration phases of flow with acceleration time, measured as the time from onset of flow to peak frequency corrected for cycle length, separated CAo patients from normal subjects. In contrast, doppler frequency distributions from the ascending aorta did not distinguish CAo from controls. In conclusion, gated pulsed doppler examination of the thoracoabdominal aorta displayed a frequency distribution specific for coarctation of the aorta. The discrepancy between ascending and descending frequency distributions represents systolic loading and diastolic decompression of the obstructed proximal thoracic aorta. This method can provide a useful adjunct to serial follow-up of coarctation patients and early detection of recoarctation.

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INFLUENCE OF  $\alpha$ -BLOCKING DRUGS PRAZOSIN (Pz), PHENTOLAMINE (Phe), AND TOLAZOLINE (T) ON CARDIOPULMONARY RESPONSE TO DOPAMINE IN AWAKE LAMBS

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Combination vasodilator and cardiotoxic therapy may help infants with pulmonary vasospasm and low cardiac output. To test the relative effectiveness of  $\alpha$ -blockers with different receptor actions, we instrumented newborn lambs with catheters to measure pressure in the pulmonary artery (PAP), aorta (SAP) and left atrium (LAP). The ductus arteriosus was tied and a flow transducer placed around the main PA. After recovery, all lambs were studied in room air on two successive days. Dopamine dose response to 2.7, 27 and 270  $\mu\text{g/kg/min}$  was measured then repeated with Phe (1 mg/kg, n=5), Pz (1 mg/kg, n=6), or T (5 mg/kg/hr, n=13). Dopamine raised SAP, PAP, LAP, systemic vascular resistance (SVR), and heart rate (HR) ( $p < .05$ ) at medium and high doses. Pulmonary vascular resistance (PVR) rose at the top dose ( $p < .01$ ) while QP didn't change and PVR/SVR fell ( $p < .01$ ). Only Phe changed basal values, lowering SAP ( $75 \pm 2$  to  $67 \pm 3$ ,  $p < .05$ ), and raising HR ( $208 \pm 20$ , to  $256 \pm 28$ ,  $p < .01$ ). All drugs blocked dopamine-induced SAP and SVR rise and allowed increased QP, HR and PVR/SVR relative to dopamine alone ( $p < .05$ ). Pz and T blunted the dopamine-induced PAP increase, which Phe did not; PVR was lower when T was coupled with dopamine ( $p < .025$ ). With Pz and Phe, PVR was the same as dopamine alone. Thus, all three drugs prevented dopamine interaction with systemic  $\alpha$ -receptors, all increased HR and cardiac output when coupled with dopamine. None completely blocked dopamine's pulmonary circulatory effect although T blunted it. Thus, all  $\alpha$ -blockers can facilitate the cardiotoxic effect of high dose dopamine, but none completely ablates its pulmonary vasoconstrictor effect. T may be more advantageous in this regard, perhaps because of its non-adrenergic effects