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DIGOXIN TOXICITY ASSOCIATED WITH LOW DOSAGE MAINTENANCE THERAPY IN PREMATURE INFANTS. Nirmala S. Desai, Thomas H. Pauly, Gregory L. Johnson, M. Douglas Cunningham, Carol M. Cottrill, Jacqueline A. Noonan. U. of Kentucky Dept. of Pediat., Lexington, Kentucky.

Current recommendations for the administration of Digoxin (DIG) to low birthweight (LBW) infants are ill defined. We report the frequent occurrence of DIG toxicity in LBW infants treated with low dose maintenance DIG: 10 µg/kg/da without an initial loading dose. DIG was administered parenterally within the first 10 days of life to 34 infants <2500 gm with signs of congestive heart failure and patent ductus arteriosus. Ten of 34 (29.4%) developed DIG toxicity diagnosed on the basis of cardiac arrhythmias, ileus, abdominal distension and/or serum DIG levels >2.0 ng/dl (range 2.1-6.1). Sixteen of the 34 were 1500-2500 gm; 2/16 (12.5%) developed signs and symptoms of DIG toxicity and had elevated serum levels. Eighteen of the 34 infants were <1500 gm with 8/18 (44.4%) becoming DIG toxic. Two infants <1500 gm died; both had toxic serum levels at the time of death and 1 died of unexplained cardiac arrhythmias. All 10 DIG toxic infants had PR intervals >.12 sec (range .13 - .18) at the time of diagnosis without evidence of electrolyte imbalance, liver or renal compromise.

We conclude that LBW infants, especially those <1500 gm, are exquisitely sensitive to DIG even at low maintenance dosage. Prolongation of PR interval was indicative of DIG toxicity in our patients. Continuous monitoring of the PR intervals and serial serum DIG levels are recommended for the avoidance of serious complications of DIG therapy in LBW infants.

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EVALUATION OF PATIENTS WITH THALASSEMIA BY ECHOCARDIOGRAPHY

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Echocardiographic studies in 44 subjects with thalassemia major(Thal) aged 5-27 years with body surface area(BSA) 0.8-1.9M² were compared to 54 normals(N) of similar age and BSA. Hemoglobin of the Thals was maintained by transfusion at 11.4 gms.% ± 3.2 S.D. Of 39 Thals(Group 1) studied prior to Desferrioxamine therapy only 1 was on therapy for heart failure. Five patients (Group 11) aged 9-15 years were studied to assess left ventricular(LV) function because of recent onset of failure. In comparison to normal data 95% confidence limits, Group 1 subjects had increased LV end diastolic dimension(LVD) in 23/39(59%) and increased left atrial dimension(LAD) in 21/39(54%); LV wall thickness was above the mean normal values in 33/39(85%) patients. In Group 11, normal data 95% confidence limits were exceeded in 4/5 for LVD and 5/5 for LAD. Remarkably good LV function was found in Group 1 subjects, including 9 over 20 and 22 over 15 years of age. However, once heart failure was apparent(Group 11), LV function was markedly reduced and despite treatment for failure progression to death occurred within 1-11 months.

	Ejection Fraction	Mean Vcf LV	%ΔLVD
N	0.72 ± 0.11	1.17 ± 0.43	35.5 ± 8.9
1	0.70 ± 0.10 NS	1.19 ± 0.34 NS	33.8 ± 8.3 NS
11	0.43 ± 0.25 <0.001	0.62 ± 0.32 <0.001	17.0 ± 12.8 <0.001

Mean ± 2 S.D.; Vcf - velocity circumferential fiber shortening

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RIGHT VENTRICULAR ENDOCARDIAL ACTIVATION MEASURED BY CATHETER TECHNIQUE: VALUES IN CHILDREN AND INFLUENCE OF HIGH AND LOW FILTERS. Macdonald Dick, Thomas J.

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To determine right ventricular (RV) endocardial activation (surface ECG to fast deflection of intracardiac electrogram) we measured activation of (a) right ventricular apex (RVA) (N=34), (b) right ventricular outflow (RVO) (N=6) and (c) right ventricular inflow (RVI) (N=3) using closely spaced (2mm) bipolar electrode catheter. Catheter positions were verified by biplane fluoroscopy with a C-arm rotated in the horizontal plane. Median age of children studied was 10 yrs (range 0.5-20.8). None had right bundle branch block (RBBB) on surface ECG. Using frequency band pass (15-300 Hz) RVA was 25.9±8.2 msec (10-42) and did not correlate with either age or RV pressure. RVI was 44.7±9.8 msec (39-56) and was 68% longer than RVA. RVO was 50.7±11.0 msec (33-66) and was 89% longer than RVA. The influence of high (150-1000 Hz) and low (15-300 Hz) filters on RVA was evaluated in 13 of these patients and 6 others with RBBB. RVA at high frequency band was on the average 1.2 msec shorter than and correlated well (r=.96) with RVA at the low frequency range.

We conclude that RV endocardial activation, measured at cardiac catheterization, proceeds in the expected manner and time course, with no clinically important difference between RVA recorded at high and low frequencies. Thus the method may be useful in defining RV endocardial activation disturbances prior to and after intracardiac surgery for congenital heart disease.

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MYOCARDIAL EXTRACTION OF OXYGEN AND CARBOHYDRATES IN THE LAMB FETUS IN UTERO. David J. Fisher, Abraham M. Rudolph, Michael A. Heymann. Cardiovascular Research

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Although fetal arterial levels of oxygen and glucose are less than half adult levels there is no information about tissue extraction of these substrates in the intact fetus. We studied fetal myocardial extraction of oxygen, glucose, lactate and pyruvate in 12 fetal lambs in utero, 1-4 days post-op. We placed catheters in inferior vena cava, carotid artery (CA), and coronary sinus (CS) via the hemiazygous vein. From simultaneously withdrawn blood, CA and CS O₂ content, blood glucose, lactate and pyruvate were measured. Myocardial blood flow (cc/min/100g) of left ventricle (MBF/min/100gLV) was calculated by the nuclide-labelled microsphere method. Myocardial extraction of substrate/min/100g of left ventricle (MV/min/100gLV) was calculated as CA minus CS level of each substrate (Δ-AV) times MBF/min/100gLV. MBF/min/100gLV was 166±19 (mean±SEM), twice the value for normal adult humans and dogs. CA levels of O₂, glucose, lactate and pyruvate (µM/L) were 3244±199, 1069±122, 2120±327 and 117±14, respectively. Δ-AV for O₂, glucose, lactate and pyruvate (µM/L) were 2117±100, 99±18, 524±88, and 49±9, half the value of normal adults. MV/min/100gLV (µM/L) for O₂, glucose, lactate and pyruvate were 333±30, 18±4, 76±16, and 7±2, respectively, equal to values for normal adults. We conclude that fetal myocardial extraction/min/100gLV of O₂ and glucose are equal to values obtained from healthy adults, despite the lower arterial levels of O₂ and glucose present in utero. This is accomplished by higher fetal myocardial blood flow.

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MYOCARDIAL NECROSIS IN STRESSED NEWBORNS. William H. Donnelly, Richard L. Bucciarelli, Robert M. Nelson.

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The recent association of transient tricuspid insufficiency of the newborn with papillary muscle necrosis prompted a detailed retrospective clinical and histologic analysis of all autopsied infants to find sites of myocardial necrosis. In a four year period, 19 of 80 autopsied infants who died within 7 days of birth were found to have one or more sites of significant myocardial damage. None of the 80 had congenital heart disease. 10/19 pregnancies were classified as high risk. All were singleton births. Of 9/19 monitored during labor, 7 had abnormal monitor patterns. Seven infants had tricuspid insufficiency (TI) murmurs and one had the murmur of mitral insufficiency (MI). All those with the TI murmurs had distinct necrotic foci in the tricuspid valve papillary muscles. The infant with the MI murmur had moderate to severe damage of the mitral valve papillary muscles. Six of seven with TI murmurs were term infants. Thirteen of 19 had suffered asphyxia, 6 of them had had massive aspiration of meconium stained amniotic fluid. Six of nineteen infants had creatine phosphokinase studies and 5 of 6 had significant elevation of the MB fraction. The occurrence of a severe asphyxial episode or abnormal monitor pattern associated with the development of TI or MI murmurs and elevated CPK-MB fraction suggests that the infant has suffered a papillary muscle or other myocardial necrosis.

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LIMITED CARDIAC RESPONSES TO STRESS IN THE NEWBORN.

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The unique fragility of the neonatal circulation in response to disease states and various physiological stimuli is apparent clinically although underlying mechanisms have not been explored. Accordingly, this report examines and compares the influence on cardiac performance of changes in left ventricular (LV) filling pressure in six conscious, unsedated newborn lambs studied serially at one and three weeks of age and five adult sheep. All animals were instrumented chronically to assess LV internal dimensions and pressures and cardiac output. At constant heart rate, infusion of saline to comparably high LV end diastolic pressures was associated in the younger newborns with significantly elevated mean arterial pressures, reduced LV stroke volume, stroke work and mean fiber shortening when compared to older newborns or adults. A separate analysis of the LV pressure-dimension relationships showed lowest LV compliance in the youngest animals with a progressive increase with age. Thus, these results suggest that the youngest newborns have limited preload reserve related to reduced LV compliance. With volume infusion sarcomeres are stretched fully; the rise in peripheral resistance creates a mismatch between afterload and the level of inotropic state. These findings provide a framework for viewing cardiocirculatory adaptation to left-to-right shunt lesions in the human newborn and support the contention that age-dependent, disadvantageous myocardial mechanical factors play a critical role in their clinical course.