127 INFLUENCE OF AGE ON LAMB LEFT VENTRICULAR POSTERIOR WALL WEIGHT, ECHO THICKNESS, AND CONTRACTION-RELAXATION SEQUENCES

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To evaluate these relationships and validate accuracy of echo in close chested lambs, echo thickness of the left ventricular posterior wall (LVPW), echo contraction-relaxation sequences and LVPW post mortem weight were measured in 37 normal sheep aged 1 day-60 weeks (mean=15.4±12.3(SD)). High quality LVPW echoes were recorded at chordal level and incremental LVPW thickness at normalized times during contraction and relaxation were measured by computer. Within 5 days of the echo, diastolic arrest was produced with potassium and LVPW was weighed after perfusion fixation with glutaraldehyde. LVPW weight and its echo thickness at 100% relaxation were linearly related to age (r=.90, SEE=7.5, r=.78, SEE=6.8 respectively) and to each other (r=.71, SEE=7.9). In all animals, irrespective of age, contraction was nearly linear; however, relaxation was fast with 71±1.9%(SE) total relaxation completed in 40% diastole. We conclude that in normal lambs <60 weeks, LVPW weight and its echo thickness increase linearly with age; LVPW echo measurements estimate actual LVPW weight; and echo contraction-relaxation sequences, similar in newborn and older sheep, imply adequate LV function at birth. Echo provides accurate data on lamb LV weight and function previously available only by invasive or post mortem exams. This new application of echo should be useful in serial sheep studies.

128 THE ROLE OF PATENT DUCTUS ARTERIOSUS (PDA) IN THE NEONATE WITH SEVERE RESPIRATORY DISEASE: A PROSPECTIVE STUDY.

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Serial aortic contrast echocardiographic studies (ACE) and differential blood gases were performed on 164 neonates with respiratory distress (149 preterm, 10 fullterm, BW=1569±421) to determine the incidence and natural history of PDA and its influence on respiratory disease. Infants were divided into three groups: (A) Spontaneous closure (SC)≤24 hrs.(B) SC≤72 hrs. (C) PDA persisting≥72 hrs. 5 neonates with open PDA died prior to 72 hrs. Results are summarized in the following table:

	N	DIED	LATE SC	REOPEN	RX CHF	RX[1] PDA	DAYS ON RESPIRATOR*	CHRONIC LUNG DISEASE*
A	18	1	--	0	0	0	1.5+1.6	3
B	53	0	--	0	0	0	1.8+4.2	10
C	88	15	34	--	70	47	9.7+9.6	41

[1] Surgery and/or Indomethacin *p < .001 A and B vs. C

While the proportion of infants ≤ 1200 gm was greatest in C, differences in outcome were not related to birth weight. The documentation of PDA closure by ACE generally preceded clinical improvement in respiratory status and appeared to represent functional closure. Spontaneous closure of PDA prior to 72 hrs. was a good prognostic sign whereas persistence of PDA after 72 hrs. was associated with a protracted course. These data suggest that early intervention (≤ 72 hrs.) for PDA may be helpful in the management of neonates with severe respiratory disease.

129 NONINVASIVE DETERMINATION OF SYSTEMIC RESISTANCE AND CARDIAC OUTPUT FROM THE ARTERIAL PRESSURE WAVEFORM

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The exponential decay of the diastolic portion of the arterial pressure waveform (APW) is characterized by a time constant τ. According to the Windkessel model of the circulation, τ should equal the product of the peripheral resistance R and the arterial capacitance C ($\tau = RC$). In four children in whom R was pharmacologically manipulated (up to twofold) during cardiac catheterization, we obtained C a total of thirty times by simultaneously determining τ from the APW and R from thermodilution cardiac output measurements. In each patient we tested whether C varied with R using t statistics. We found that in fact there was no significant variation of C with R, within a 95% confidence range. Since C is constant in a given patient, the variation in τ is directly proportional to the variation in R. Similarly, the variation in cardiac output is proportional to the variation in the quantity $\Delta P/\tau$, where ΔP is the mean arterio-venous pressure difference. Analysis of the arterial pressure waveform to determine mean arterial pressure and the diastolic decay time constant τ thus provides a noninvasive means of monitoring changes in both peripheral resistance and cardiac output.

130 NUCLEOPROTEIN COMPOSITION OF THE HEART OF THE CARDIOMYOPATHIC TURKEY.

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We examined the possible involvement of nuclear proteins in the pathogenesis of a naturally occurring model of congestive cardiomyopathy(CCM) in turkeys. The protein composition of myocardial nuclei was compared in CCM (n=18) and control (n=9) turkeys, 70-140 days old. CCM hearts as a group had a higher histone content (1.75+0.09(SD) mg/g vs 1.65+0.07 in Con, P<0.01) and histone/nonhistone protein ratio (1.07+0.07 vs 0.95+0.02, P<0.01). The latter was independent of age and correlated well (r=0.89) with the degree of cardiac dilation. The electrophoretic pattern of chromatin proteins did not differ in the two experimental groups. In vitro phosphorylation of nuclei was decreased in CCM hearts (9.7+0.2 vs 12.8+0.1 pmole ^{32}/mg prot/15 min, P<0.01). The decrease was due to lower NHP phosphorylation (5.78+1.38 vs 8.33+0.81 pmole ^{32}P/mg prot/15 min, P<0.01). DEAE-Sephacel chromatography separated cyclic AMP-dependent and independent nuclear protein kinases. Lower cAMP-independent activities were present in CCM hearts. There was a significant linear correlation between NHP phosphorylation and degree of cardiac dilation (r=0.75) or contractility as reflected by left ventricular systolic time intervals (r=0.79). SDS-polyacrylamide gel electrophoresis of phosphorylated nucleoproteins revealed differences in the lower molecular weight species of NHPs between control and CCM hearts. These results suggest that development of this cardiomyopathy is associated with, and may be secondary to, changes in the composition and function of myocardial nucleoproteins.

131 EFFECT OF DIGOXIN ON MORTALITY AND ON BLOOD FLOW DISTRIBUTION IN THE CARDIOMYOPATHIC TURKEY.

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Congestive cardiomyopathy(CCM) of turkeys(TK) results in a 25-30% mortality by 10 days of age in our inbred flock. We examined the effect of oral digoxin(Dig) (0.05 mg/kg/day) on the early mortality, and the effect of IV Dig (0.1 mg/kg) on blood flow (BF) distribution in inbred TK with and without cardiac dilation. Dig reduced mortality from 28.3% (28/99) in untreated CCM TK to 9.2% (6/65) in treated TK (P<0.01). Radionuclide labeled spheres ("15" μm) were used to measure BF during control conditions and again 10 min following IV Dig in 10 TK without (Con) and 9 TK with significant cardiac dilation(CD) at a mean age of 113 days (range 76-167 days). Mean systemic pressure was reduced in CD TK (134+5 (SE) vs 182+13 mmHg, P<0.01). Control values for right and left ventricular(LV), renal, hepatic, pancreatic, intestinal, and skeletal muscle. BF (ml/min/g) in CD TK were similar to values of 1.83+0.27, 3.00+0.30, 2.22+0.17, 1.41+0.23, 2.37+0.38, 2.09+0.24, and 0.47+0.005, resp, in Con TK, P>0.05. Of particular interest, the LV subendo-subepicardial BF ratio was similar in Con and CD TK (1.34+0.04 vs 1.26+0.03). Dig had no effect on total or regional myocardial BF in CD or Con TK; it did significantly reduce renal (-24%, P<0.005), hepatic (-27%, P<0.025) and pancreatic (-32%, P<0.01) BF in Con TK. The results of this study suggest that Dig, by unknown mechanism(s) reduces early mortality in CCM TK; that the transmural distribution of LV flow in 3-4 month TK with cardiac dilation is not altered; and that Dig has no effect on regional BF distribution in myopathic hearts.

132 ACTION POTENTIAL CHANGES IN CARDIOMYOPATHIC TURKEYS.

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Arrhythmias are commonly observed in turkey poults(TK) inbred for congestive cardiomyopathy(CCM). We examined the possibility that alterations of transmembrane action potentials(AP) in left(LV) and right ventricular(RV) muscle fibers from CCM TK might contribute to development of arrhythmias. Resting membrane potential (RMP), AP amplitude, maximum rate of AP phase 0(dV/dt max) and APD_{90} in LV tissue (35°C) from CCM hearts as a group did not differ significantly vs control(Con) hearts; APD_{50}, however, was reduced in myopathic LV (201+6(SE) msec vs 228+9 in Con, P<0.05). In RV tissue, RMP was increased (P<0.01), and both APD_{50} (186+5 msec vs 206+4 in Con, P<0.01) and APD_{90} (208+4 msec vs 228+3 in Con, P<0.01) were shortened in CCM hearts. Since severity of cardiac dilation and hypertrophy may vary in CCM TK, the effects of hypertrophy on AP characteristics were examined. The only AP characteristic which distinguished LV tissue from CCM hearts with significant hypertrophy (ie 80% increase in heart/body wt ratio) from LV tissue in CCM TK without hypertrophy, was a reduced dV/dt max in the former (98+6 vs 274+26 V/sec, P<0.01). On the other hand, dV/dt max in hypertrophied and Con RV were similar while APD_{50} and APD_{90} in hypertrophied RV were shortened (174+7 vs 202+6 msec, P<0.01; 193+6 vs 224+5 msec, P<0.01). In summary, this study has identified AP abnormalities in ventricular muscle cells which may be associated with the occurrence of arrhythmias in this model of congestive cardiomyopathy.