● 193 THE INOTROPIC EFFECT OF OUABAIN ON THE NEWBORN MYOCARDIUM DURING REOXYGENATION FOLLOWING HYPOXIA

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The effect of ouabain on myocardial mechanical function was studied during reoxygenation (re-O_2) following 40 min of hypoxia in 8 newborn (NB) rabbits and the results were compared with those obtained in 9 NB control rabbits (without hypoxia). All studies were performed in the isolated, arterially perfused hearts. The hearts were perfused with Krebs-Henseleit (K-H) solution, maintained at 27°C, and paced at 36 beats/min. The muscles were initially perfused with oxygenated solution, and then perfused with hypoxic solution. After 40 min of hypoxia, oxygenated solution was reinstituted. Ouabain was infused during re-O_2 after mechanical function reached a steady state (approximately 20 min after re-O_2). Paired electrical stimulation was also performed before hypoxia and after re-O_2 (N=5). Parameters of mechanical function were recorded continuously. +dT/dt (max) decreased significantly during hypoxia and returned to control value during re-O_2. The positive inotropic effect of paired electrical stimulation after re-O_2 (156 ± 7% of control) was not significantly different from that in the control group (168 ± 8%). Inotropic effect of ouabain during re-O_2 (52 ± 7% of control) was significantly (p=0.02) less than that in the control group (95 ± 16%). These data suggest that the inotropic effect of ouabain is reduced in the reoxygenated NB heart after hypoxia and this is not due to a change in excitation-contraction coupling.

194 CARDIOVASCULAR EFFECTS OF PERINATAL ASPHYXIA IN FULL-TERM INFANTS.

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The cardiovascular effects of severe perinatal asphyxia was studied during the first 3 days of life by serial measurements of arterial blood pressure (ABP), central venous pressure (CVP) and M-mode echocardiograms in 10 fullterm infants (B.Wt. 3482 ± 214g, G.A. = 40.5 ± 0.98 wks. one minute Apgar Score = 2.2 ± 0.44) and was compared to 10 healthy infants matched for B.Wt. and G.A. During the first 8 hours of life, ABP (mean ± S.E.) in asphyxiated infants was 44.8 ± 2.4 mmHg, RPEP/RVET was 0.61 ± 0.07, LPEP/LVET was 0.40 ± 0.03 and the echocardiographically derived LV stroke volumes (LVSV) was 4.9 ± 0.66 ml and the aortic ejection area (AEA) was 97 ± 5 Cm-Msec. In the healthy infants, the corresponding values were: APB = 48.3 ± 1.8 mmHg, RPEP/RVET = 0.38 ± 0.03, LPEP/LVET = 0.33 ± 0.01, LVSV = 5.8 ± 0.31 ml and AEA = 127 ± 6 Cm-Msec. Except for elevated RPEP/RVET, there were no significant differences between asphyxiated and healthy infants at 24 and 48 hours of life. All asphyxiated infants had normal CVP for the first 8 hours and only one who subsequently expired, developed elevated CVP beyond the 24 hours of life. The presence LV failure and pulmonary hypertension in the absence of RV failure during the immediate post-partum period further supports the evidence for the vulnerability of LV during the transitional circulation and its contributory role in the genesis of the persistent pulmonary hypertension of the newborn.

● 195 MYOCARDIAL BLOOD FLOW (Q) AND O_2 CONSUMPTION ($\dot{V}O_2$) DURING ACUTE HYPOXEMIA IN NEWBORN LAMBS.

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We previously showed that myocardial Q and left ventricular (LV) $\dot{V}O_2$ at rest are higher in neonatal lambs than in fetal or adult sheep. To determine whether the neonate has similar reserve to further increase myocardial Q and O_2 supply during hypoxemia, we measured myocardial Q and LV $\dot{V}O_2$ in 5 lambs (4-5 days) three days after thoracotomy, before and during hypoxia (FIO_2=0.09). Myocardial Q was measured by the microsphere method; LV $\dot{V}O_2$ was calculated from Q and the O_2 content difference between aortic and coronary sinus (CS) blood (LV(A-V)). LV work was estimated from the rate-pressure product. Hypoxia produced a 51% decrease in arterial O_2 content, a 16% increase in cardiac output, and a 46% increase in LV work. Although CS O_2 content fell and myocardial O_2 extraction coefficient increased (.62 vs .66), LV(A-V) decreased 47%. LV $\dot{V}O_2$ increased 27% because of a 139% increase in LV Q (183 vs 438 ml/100g). Right ventricular Q (126 vs 451 ml/100g) increased even more, probably because of the increase in pulmonary arterial systolic pressure (24 to 41 mmHg). Despite the increase in heart rate there was only a small decrease in inner:outer flow ratio (1.14 to 0.97 in LV, and 1.22 to 1.1 in right ventricle). Our studies show that despite high resting values there is considerable reserve for increasing flow to the neonatal myocardium. This reserve allows the LV to increase its O_2 supply and $\dot{V}O_2$ during severe hypoxemia and therefore to increase its work and output without subendocardial ischemia and probably without anaerobic metabolism.

● 196 PROCAINAMIDE ELIMINATION KINETICS IN PEDIATRIC PATIENTS.

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Procainamide (PA) is a common antiarrhythmic used in pediatrics, yet little is known about its kinetics in children. We examined PA elimination kinetics following a single intravenous dose (range 4-30 mg/kg) in 5 patients (pts), ages 6-16 yrs, (ventricular tachycardia 3 pts, atrial flutter 2 pts). Serial blood samples were analysed for PA and N-acetyl procainamide (NAPA) by a gas chromatographic assay. PA concentration-time curves fit a two compartment model and the following pharmacokinetic parameters were calculated: distribution half-life, $T_{½}\alpha$ = 0.16 ± 0.09 (mean ± S.D.) hr; elimination half-life, $T_{½}\beta$ = 1.99 ± 0.37 hr; apparent volume of distribution, V_D = 2.34 ± 0.42 L/Kg; elimination rate constant, K_E = 1.23 ± 0.54 hr^{-1} and plasma clearance, P_{CL} = 14.97 ± 4.51 ml/min/kg. NAPA levels peaked 2.04 ± 1.21 hr after PA administration and the elimination half-life was 3.5 ± 1.1 hr. The elimination half-life for PA in our patients is significantly lower than that reported in healthy adult volunteers (1.99 ± 0.37 vs 2.80 ± 0.44 hr; $p < 0.05$) whereas, the volume of distribution is higher (2.34 ± 0.42 vs 1.98 ± 0.84 L/Kg, $p < 0.05$). The short PA elimination half-life appears to be related to a significantly higher plasma clearance in children (14.97 ± 4.51 vs 5.86 ± 1.26 ml/min/kg, $p < 0.02$). Thus, pediatric patients should require relatively higher doses and/or shorter dosing intervals, as compared to adults, to achieve therapeutically effective blood levels of PA.

197 ECHOCARDIOGRAPHIC FINDINGS IN CEREBRAL ARTERIOVENOUS MALFORMATIONS (AVM)

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Five newborns (mean weight 3.5 Kg) with cerebral AVM were evaluated by M-mode echocardiography (E). Two died without surgery, 1 intraoperatively, and 1 ten months post-operatively (PO). The fifth is alive 2 years PO with severe neurological damage. Initial E revealed mild right ventricular (RV) dilatation with an end diastolic dimension (EDD) of 1.9±.96cm. and normal septal motion. A normal left ventricular (LV) EDD of 1.98±.32 and an end diastolic volume index (EDVI) of 41.6±19.6 increased subsequently to 2.29±.26 and 59.2±2.31 on the 3 patients (pts.) examined just prior to surgery at 20-60 days of age. PO the 2 survivors had a markedly diminished LV EDVI of 24.7±6.2 and the RV diameter was .413±.21. Thus these pts. had E evidence of biventricular volume overload pre-operatively compared with PO, however, the pre-operative LV size was still in the normal range for normal infants. All but 1 pt. had an easily seen, large descending aorta on E. In utero most of the AVM return would be shunted via the ductus away from the LV and down the descending aorta. Thus the LV would be relatively small and unprepared for the massive increase in flow associated with the ex-utero circulation and the descending aorta would be large. Our E findings are consistent with this explanation. The relatively undilated LV at birth would be partly responsible for the inability of these infants to tolerate the acute volume overload and their early severe congestive heart failure.

198 IS MYOCARDIAL HYPERTROPHY IN HYPERTENSIVE CHILDREN RELATED TO BLOOD PRESSURE?

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The mechanism for the increase in left ventricular mass (LVM) in children with labile hypertension (HT) remains unresolved. M-mode echocardiograms (ME) were obtained from 27 HT children (mean age 14.4 y) and 26 normotensive (NT) children (mean age 14.1 y) of comparable sex, race and BSA. Mean systolic/diastolic blood pressure (SBP/DBP) in HT was 137/89; that in NT was 110/68 ($p < 0.001$). ME was digitized/analyzed with H-P computer, and the observed values expressed as SD from predicted normal (σ PN) based on age, BSA and HR. HT and NT values were similar for: LVEDD, LVESD, LA_{max}, LVSV, Qlv, LVET and PEP/ET. However, HT values were greater than NT for: wall thickness ($p < .001$), LVM ($p < .005$), thickness/radius ratio (t/r) ($p < .001$), Ao ($p < .05$) and PEP ($p < .025$). HT values were lower than NT for %MAS ($p < .01$) and VCF ($p < .05$). Poor correlation was observed between SBP or DBP and LVM/M^2 or σ LVM ($r = 0.34$ to 0.43). Density function curves derived by multi-regression analysis (using equation: $Y_{dv} = K_1\ \sigma PN_1 + K_2\ \sigma PN_2 + K_n\ \sigma PN_n \pm X$, where Y_{dv} = discriminating value and K, X = constants) and utilizing 11 echo parameters separated HT from NT with minimal overlap ($p < .001$). Moreover, positive correlation was observed between Y_{dv} and resting DBP ($r = 0.65$), suggesting that the cardiac status of HT children may very well be related to the increased pressure overload of labile character and varying duration.